preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the
	Production of ICAM-1
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			generated. Exemplary cells that	
			assays include Aortic Smooth	
			Muscle Cells (AOSMC); such	
			as bovine AUSIMC.	Highly preferred indications
HACBT91	419	Production of IL-10	Assays for production of 12-19 and activation of T-cells are	include allergy and asthma.
	-	cells.	well known in the art and may	Additional highly preferred
			be used or routinely modified to	indications include immune and
			assess the ability of	hematopoietic disorders (e.g., as
			polypeptides of the invention	described below under "Immune
			(including antibodies and	Activity", and "Blood-Related
			agonists or antagonists of the	Disorders"), autoimmune
			invention) to stimulate or inhibit	diseases (e.g., rheumatoid
			production of IL-10 and/or	arthritis, systemic lupus
			activation of T-cells.	erythematosis, Crohn"s disease,
			Exemplary assays that may be	multiple sclerosis and/or as
			used or routinely modified to	described below),
			assess the ability of	immunodeficiencies (e.g., as
			polypeptides and antibodies of	described below), boosting a T
			the invention (including agonists	cell-mediated immune response,
			or antagonists of the invention)	and suppressing a T cell-
			to modulate IL-10 production	mediated immune response.
			and/or T-cell proliferation	
			include, for example, assays	
			such as disclosed and/or cited	
			in: Robinson, DS, et al., "Th-2	
			cytokines in allergic disease" Br	
			Med Bull; 56 (4): 956-968	
			(2000), and Cohn, et al., "T-	
	,		helper type 2 cell-directed	
			therapy for asthma"	

	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication
tents tents to to to to ser of ser of ells rrete 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6. 6.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of or alt polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, indic
Pharm 88: 18 of each incorp their eithat m; these a IL10 s may be Th2 ce are a c IL4, II Factor differe Th2 ce the ini of alle yoia in polarize polarize	Activation of Assay transcription through transcr cAMP response response lement (CRE) in knowr pre-adipocytes. used o assess polype (includation)
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associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure, nephropathy	and/or other diseases and	disorders as described in the	"Renal Disorders" section	below), diabetic neuropathy,	nerve disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g.,
regulate CREB transcription factors, and modulate	expression of genes involved in	a wide variety of cell functions.	For example, a 3T3-L1/CRE	reporter assay may be used to	identify factors that activate the	cAMP signaling pathway.	CREB plays a major role in	adipogenesis, and is involved in	differentiation into adipocytes.	CRE contains the binding	sequence for the transcription	factor CREB (CRE binding	protein). Exemplary assays for	transcription through the cAMP	response element that may be	used or routinely modified to	test cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch et	al., Mol Cell Biol 20(3):1008-	1020 (2000); and Klemm et al.,	J Biol Chem 273:917-923	(1998), the contents of each of
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infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in
	Activation of transcription through cAMP response element (CRE) in pre-adipocytes.
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(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section	below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke,	neuropathy or blood vessel blockage), seizures, mental	confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other	described in the "Cardiovascular	Disorders" section below), dyslipidemia, endocrine	disorders (as described in the "Endocrine Disorders" section		impairment (e.g., diabetic	retinopathy and blindness), ulcers and impaired wound	healing, and infection (e.g.,		Diseases" section below,
a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the	cAMP signaling pathway. CREB plays a major role in adinogenesis and is involved in	differentiation into adipocytes. CRE contains the binding	sequence for the transcription factor CREB (CRE binding protein). Exemplary assays for	transcription through the cAMP response element that may be	used or routinely modified to test cAMP-response element	activity of polypeptides of the invention (including antibodies	and agonists or antagonists of	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	85:6342-6346 (1988); Reusch et	al., Mol Cell Biol 20(3):1008-	1020 (2000); and Klemm et al., J Biol Chem 273:917-923	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. Fre-adinocytes that may be used
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especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"), Preferred indications include autoimmune diseases (e.g.,
according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
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rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described	below) and immunodeficiencies (e.g., as described below).	Preferred indications include neoplastic diseases (e.g.,	leukemia, lymphoma,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary tract cancers	"Hyperproliferative Disorders").	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,				and tissues, hemophilia,
invention) to regulate GATA3 transcription factors and modulate expression of mast	cell genes important for immune response development.	Exemplary assays for transcription through the	GATA3 response element that	modified to test GATA3-	response element activity of	polypeptides of the invention	(including antibodies and agonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell et	al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur J	Immunol 29(12):3914-3924	(1999); Zheng and Flavell, Cell	89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by reference	in its entirety. Mast cells that	may be used according to these
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hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies
assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
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(e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary tract cancers and/or as described below under "Hynernroliferative Disorders").	Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example,	hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease,	acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel		hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to	test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., I Immunol 165(12):7215-	7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the	contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available	(e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1

				mennus, endocardius,
				meningitis, Lyme Disease,
		-		asthma and allergy.
HADD113	421	Activation of	Assays for the activation of	Highly preferred indications
	<u> </u>	transcription through	transcription through the	include neoplastic diseases (e.g.,
_		GAS response	Gamma Interferon Activation	leukemia, lymphoma, and/or as
_		element in immune	Site (GAS) response element are	described below under
-		cells (such as T-	well-known in the art and may	"Hyperproliferative Disorders").
		cells).	be used or routinely modified to	Highly preferred indications
			assess the ability of	include neoplasms and cancers,
	-1-		polypeptides of the invention	such as, for example, leukemia,
			(including antibodies and	Iymphoma (e.g., T cell
			agonists or antagonists of the	lymphoma, Burkit's
			invention) to regulate STAT	lymphoma, non-Hodgkins
			transcription factors and	Iymphoma, Hodgkin"s disease),
			modulate gene expression	melanoma, and prostate, breast,
			involved in a wide variety of	lung, colon, pancreatic,
			cell functions. Exemplary	esophageal, stomach, brain,
			assays for transcription through	liver and urinary cancer. Other
			the GAS response element that	preferred indications include
			may be used or routinely	benign dysproliferative
			modified to test GAS-response	disorders and pre-neoplastic
			element activity of polypeptides	conditions, such as, for example,
			of the invention (including	hyperplasia, metaplasia, and/or
			antibodies and agonists or	dysplasia. Preferred indications
		***	antagonists of the invention)	include autoimmune diseases
			include assays disclosed in	(e.g., rheumatoid arthritis,
			Berger et al., Gene 66:1-10	systemic lupus erythematosis,
			(1998); Cullen and Malm,	multiple sclerosis and/or as
			Methods in Enzymol 216:362-	described below),
			368 (1992); Henthorn et al.,	immunodeficiencies (e.g., as
			Proc Natl Acad Sci USA	described below), boosting a T

Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	and suppressing a T cell- mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An	
	idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune	

reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting or inhibiting immune cell proliferation. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications
	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
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include boosting an eosinophil- mediated immune response, and suppressing an eosinophil- mediated immune response.	
and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by	Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human

	A highly preferred indication is diabetes mellitus. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage
Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils." J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation." J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4
	Regulation of transcription via DMEF1 response element in adipocytes and preadipocytes
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		aromoter) and to requilate	(e.g. due to diabetic
		promoter) and to regarded	neuronathy) blood vessel
 		INSUIIII production. The	hockage heart disease, stroke,
		present in the GLIT4 promoter	impotence (e.g., due to diabetic
 		and binds to MEF2 transcription	neuropathy or blood vessel
		factor and another transcription	blockage), seizures, mental
		factor that is required for insulin	confusion, drowsiness,
		regulation of Glut4 expression	nonketotic hyperglycemic-
-		in skeletal muscle. GLUT4 is	hyperosmolar coma,
		the primary insulin-responsive	cardiovascular disease (e.g.,
		glucose transporter in fat and	heart disease, atherosclerosis,
	-	muscle tissue. Exemplary assays	microvascular disease,
		that may be used or routinely	hypertension, stroke, and other
 		modified to test for DMEF1	diseases and disorders as
-		response element activity (in	described in the "Cardiovascular
		adipocytes and pre-adipocytes)	Disorders" section below),
		by polypeptides of the invention	dyslipidemia, endocrine
 -		(including antibodies and	disorders (as described in the
		agonists or antagonists of the	"Endocrine Disorders" section
		invention) include assays	below), neuropathy, vision
		disclosed in Thai, M.V., et al., J	impairment (e.g., diabetic
		Biol Chem, 273(23):14285-92	retinopathy and blindness),
		(1998); Mora, S., et al., J Biol	ulcers and impaired wound
 		Chem, 275(21):16323-8 (2000);	healing, and infection (e.g.,
		Liu, M.L., et al., J Biol Chem,	infectious diseases and disorders
		269(45):28514-21 (1994);	as described in the "Infectious
		"Identification of a 30-base pair	Diseases" section below,
		regulatory element and novel	especially of the urinary tract
		DNA binding protein that	and skin). An additional highly
		regulates the human GLUT4	preferred indication is obesity
		promoter in transgenic mice", J	and/or complications associated
 _		Biol Chem. 2000 Aug	with obesity. Additional highly
		4;275(31):23666-73; Berger, et	preferred indications include

weight loss or alternatively, weight gain. Additional highly preferred indications are	complications associated with insulin resistance.									Preferred embodiments of the	invention include using polypeptides of the invention (or	antibodies, agonists, or	antagonists thereof) in detection,	diagnosis, prevention, and/or	hypersensitivity and	inflammation.
al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Fnzymol. 216:362–368 (1992).	the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and	pre-adipocytes that may be used according to these assays are publicly available (e.g., through	the ATCC) and/or may be routinely generated. Exemplary cells that may be used according	to these assays include the mouse 3T3-L1 cell line which is	an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells	are a continuous substrain of 3T3 fibroblasts developed	through clonal isolation. These	cells undergo a pre-adipocyte to adipose-like conversion under	appropriate differentiation culture conditions.	Caspase Apoptosis. Assays for	caspase apoptosis are well known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(IIICIUUIII) airii oo o	invention) to regulate caspase
										Regulation of	apoptosis of immune	cells).				
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protease-mediated apoptosis in	immune cells (such as, 10f example, in mast cells). Mast	cells are found in connective	and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -antigen,	promoted by 1 neiper cell type 2	cytokines, is an important	Dysregulation of mast cell	apoptosis may play a role in	allergic disease and mast cell	tumor survival. Exemplary	assays for caspase apoptosis that	may be used or routinely	modified to test capase	apoptosis activity induced by	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in: Masuda A, et al., J	Biol Chem, 276(28):26107-	26113 (2001); Yeatman CF 2nd,	et al., J Exp Med, 192(8):1093-	1103 (2000);Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the contents	of each of which are herein
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	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as
incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists or antagonists of the invention) include the assays disclosed in
·	Activation of Natural Killer Cell ERK Signaling Pathway.
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described below under "Immune Activity", "Cardiovascular	Disorders', and/or "Blood- Related Disorders"), immune	disorders (e.g., as described	below under "Immune Activity") and infections (e.g.,	as described below under	"Infectious Disease").	Preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary cancer, lymphoma	and leukemias. Other preferred
Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis	JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin,	Nature 410(6824):37-40 (2001);	and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500	(1999); the contents of each of	which are herein incorporated	by reference in its entirety.	Natural killer cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC). Exemplary	natural killer cells that may be	used according to these assays	include the human natural killer	cell lines (for example, NK-YT	cells which have cytolytic and	cytotoxic activity) or primary	NK cells.												
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indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis
	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
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		A highly preferred	A nigniy piciciou
the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit	Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each	by reference in its entirety.	IFINGAMMA FIMIA I. IFING Plays
		Dendingtion of	Production of
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,		IEN gomma neing a	a central role in the immune	embodiment of the invention
01			e a	includes a method for
				stimulating the production of
			IFNg promotes TH1 and	IFNg. An alternative highly
			inhibits TH2 differentiation;	preferred embodiment of the
			promotes IgG2a and inhibits IgE	invention includes a method for
		,	secretion; induces macrophage	ing th
-			activation; and increases MHC	IFNg. Highly preferred
			expression. Assays for	indications include blood
			immunomodulatory proteins	disorders (e.g., as described
			produced by T cells and NK	below under "Immune
	1 <u>-</u>		cells that regulate a variety of	Activity", "Blood-Related
			inflammatory activities and	Disorders", and/or
			inhibit TH2 helper cell functions	"Cardiovascular Disorders"),
-			are well known in the art and	and infection (e.g., viral
			may be used or routinely	infections, tuberculosis,
			modified to assess the ability of	infections associated with
			polypeptides of the invention	chronic granulomatosus disease
			(including antibodies and	and malignant osteoporosis,
			agonists or antagonists of the	and/or as described below under
			invention) to mediate	"Infectious Disease"). Highly
			immunomodulation, regulate	preferred indications include
			inflammatory activities,	autoimmune disease (e.g.,
			modulate TH2 helper cell	rheumatoid arthritis, systemic
			function, and/or mediate	lupus erythematosis, multiple
			humoral or cell-mediated	sclerosis and/or as described
			immunity. Exemplary assays	below), immunodeficiency (e.g.,
			that test for immunomodulatory	as described below), boosting a
			proteins evaluate the production	T cell-mediated immune
			of cytokines, such as Interferon	response, and suppressing a 1
			gamma (IFNg), and the	cell-mediated immune response.
			activation of T cells. Such	Additional highly preferred
			assays that may be used or	indications include

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inflammation and inflammatory disorders. Additional preferred indications include idiopathic	pulmonary tibrosis. Highly preferred indications include	neoplastic diseases (e.g.,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, 10r example, leukemia, lymphoma,	melanoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sensis neutropenia
routinely modified to test immunomodulatory activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin I ab Anal 8(5)·225-233 (1995):	Billiau et al., Ann NY Acad Sci	856:22-32 (1998); Boehm et al.,	Annu Rev Immunol 15:749-795	(1997), and Rheumatology	(Oxford) 38(3):214-20 (1999),	the contents of each of which	are herein incorporated by	reference in its entirety. Human	T cells that may be used	according to these assays may	be isolated using techniques	disclosed herein or otherwise	known in the art. Human T	cells are primary human	lymphocytes that mature in the	thymus and express a T Cell	receptor and CD3, CD4, or	CD8. These cells mediate	humoral or cell-mediated	imminity and may be
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neutrophilis neorigeis	ry factors.	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma and allergy.	475 Production of IL-13 Assays for production of IL-13	and activation of T- and activation of T-cells are	well known in the art and may		assess the ability of hematopoietic disorders (e.g., as	invention	(including antibodies and Activity", and "Blood-Related	the	invention) to stimulate or inhibit diseases (e.g., rheumatoid	 	r IL-13	production that may be used or described below),	pu	 (including agonists or and suppressing a T cell-	antagonists of the invention) mediated immune response.	include, for example, assays	include, for example, assays such as disclosed and/or cited	include, for example, assays such as disclosed and/or cited in: Grunig, G, et al.,	include, for example, assays such as disclosed and/or cited in: Grunig, G, et al., "Requirement for IL-13	include, for example, assays such as disclosed and/or cited in: Grunig, G, et al., "Requirement for IL-13 independently of IL-4 in
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Science;282: 2261-2263 (1998),	and Wills-Karp M, et al.,	"Interleukin-13: central	mediator of allergic asthma"	Science; 282: 2258-2261	(1998); the contents of each of	which are herein incorporated	by reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL13, a Th2	type cytokine, is a potent	stimulus for mucus production,	airway hyper-responsiveness	and allergic asthma. Th2 cells	are a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation of	Th2 cells play a major role in	the initiation and pathogenesis	of allergy and asthma. Primary	Thelper 2 cells are generated in	in vitro culture under Th2	polarizing conditions using	peripheral blood lymphocytes	isolated from cord blood.	This reporter assay measures activation or inhibition of the	NFkB signaling pathway in	Ku812 human basophil cell line.	Assays for the activation or
																					`						Activation or inhibition of	transcription through	NFKB response	element in immune
													-														426			
																											HAGDW20			
																												71		

inhibition of transcription	through the NFKB response	element are well-known in the	art and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	NFkB is important in the	pathogenesis of asthma.	Exemplary assays for	transcription through the NFKB	response element that may be	used or rountinely modified to	test NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone et	al, Int Arch Allergy Immunol	1114(3):207-17 (1997), the	contents of each of which are	herein incorporated by reference
cells (such as	basophils).	· (
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	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers,
in its entirety. Cells were pretreated with SID supernatants or controls for 15-18 hours, and then 10 ng/mL of TNF was added to stimulate the NFkB reporter. SEAP activity was measured after 48 hours. Basophils that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res. 9:381-390 (1985); Blom et al., Eur J Immunol. 22:2025-32 (1992), where the contents of each are herein incorporated by reference in its entirety.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of
	Activation of transcription through GAS response element in immune cells (such as T-cells).
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nolynentides of the invention	such as. for example, leukemia,
(including antibodies and	lymphoma (e.g., T cell
agonists or antagonists of the	lymphoma, Burkit's
invention) to regulate STAT	lymphoma, non-Hodgkins
transcription factors and	lymphoma, Hodgkin"s disease),
modulate gene expression	melanoma, and prostate, breast,
involved in a wide variety of	lung, colon, pancreatic,
cell functions. Exemplary	esophageal, stomach, brain,
assays for transcription through	liver and urinary cancer. Other
the GAS response element that	preferred indications include
may be used or routinely	benign dysproliferative
modified to test GAS-response	disorders and pre-neoplastic
element activity of polypeptides	conditions, such as, for example,
of the invention (including	hyperplasia, metaplasia, and/or
antibodies and agonists or	dysplasia. Preferred
antagonists of the invention)	indications include autoimmune
include assays disclosed in	diseases (e.g., rheumatoid
Berger et al., Gene 66:1-10	arthritis, systemic lupus
(1998); Cullen and Malm,	erythematosis, multiple sclerosis
 Methods in Enzymol 216:362-	and/or as described below),
368 (1992); Henthorn et al.,	immunodeficiencies (e.g., as
Proc Natl Acad Sci USA	described below), boosting a T
 85:6342-6346 (1988);	cell-mediated immune response,
Matikainen et al., Blood	and suppressing a T cell-
93(6):1980-1991 (1999); and	mediated immune response.
 Henttinen et al., J Immunol	Additional preferred indications
155(10):4582-4587 (1995), the	include inflammation and
contents of each of which are	inflammatory disorders.
herein incorporated by reference	Highly preferred indications
in its entirety. Exemplary	include blood disorders (e.g., as
mouse T cells that may be used	described below under "Immune
according to these assays are	Activity", "Blood-Related
publicly available (e.g., through	Disorders", and/or

				the ATCC). Exemplary T cells that may be used according to	"Cardiovascular Disorders"), and infection (e.g., viral
				these assays include the CTLL	infections, tuberculosis,
				cell line, which is a suspension culture of IL-2 dependent	chronic granulomatosus disease
				cytotoxic T cells.	and malignant osteoporosis,
					and/or an infectious disease as
					described below under
					"Infectious Disease"). An
					additional preferred indication is
					idiopathic pulmonary fibrosis.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas, multiple
					myeloma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted organs
					and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HAGEG10	427	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
13			IFNgamma using a	a central role in the immune	embodiment of the invention
			T cells	system and is considered to be a	includes a method for
				proinflammatory cytokine.	stimulating the production of

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e highly	int of the	invention includes a method for	ction of	Highly preferred	poold	escribed	ıne	elated		sorders"),	viral	osis,	d with	chronic granulomatosus disease	porosis,	and/or as described below under	"Infectious Disease"). Highly	is include	e (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	described	below), immunodeficiency (e.g.,	as described below), boosting a	mune	response, and suppressing a T	cell-mediated immune response.	referred	į	inflammation and inflammatory	disorders. Additional preferred	indications include idiopathic
alternative	embodime	includes a	inhibiting the production of	Highly	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	ranulomat	and malignant osteoporosis,	described	ıs Disease	preferred indications include	autoimmune disease (e.g.,	id arthritis	thematosi	sclerosis and/or as described	nmunode	woled become	T cell-mediated immune	and supp	ated imm	Additional highly preferred	indications include	ition and i	. Additio	ns include
IFNg. An alternative highly	preferred embodiment of the	invention	inhibiting	IFNg.	indication	disorders	below unc	Activity",	Disorders", and/or	"Cardiova	and infect	infections	infections	chronic gr	and malig	and/or as	"Infection	preferred	autoimm	rheumato	lupus ery	sclerosis	below), in	as describ	T cell-me	response,	cell-medi	Addition	indication	inflamms	disorders	ındıcatıo
	ou;	oits IgE				sins	¥	ty of	pu	inctions	and		ility of	ition	_	fthe		ılate		_			ssays	ulatory	duction	erferon		ch	or	±.	vity of	ntion
TH1 and	fferentiati	a and inhil	ses macro	increases	says for	atory prote	cells and]	ate a varie	ctivities a	lper cell fi	in the art	routinely	sess the ab	f the inver	bodies and	agonists o	nediate	ation, regu	activities,	helper cel	or mediate	1-mediated	emplary a	munomod	ate the pro	uch as Int), and the	cells. Su	y be used	ified to tes	latory acti	f the inve
IFNo promotes TH1 and	inhibits TH2 differentiation;	promotes IgG2a and inhibits IgE	secretion; induces macrophage	activation; and increases MHC	expression. Assays for	immunomodulatory proteins	produced by T cells and NK	cells that regulate a variety of	inflammatory activities and	inhibit TH2 helper cell functions	are well known in the art and	may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for immunomodulatory	proteins evaluate the production	of cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention
IFNo	diuhib	prom	secret	activa	expre	immr	produ	cells	inflar	dihii	are w	may	modi	poly	(inch	agon	inver	imm	infla	mod	funct	hum	imm	that	prote	ofc	gami	activ	assa	routi	imm	looly
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pulmonary fibrosis. Highly preferred indications include neoplastic diseases (e.g.,	leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative	Disorders"). Highly preferred indications include neoplasms and cancers, such as, for	example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Preferred	ndications include ancima, pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease, inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs
(including antibodies and agonists or antagonists of the invention) include the assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204 (1999); Rowland et al.,	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856-22-32 (1998): Boehm et al.,	Annu Rev Immunol 15:749-795 (1997), and Rheumatology	(Oxford) 38(3):214-20 (1999), the contents of each of which	are herein incorporated by	reference in its entirety. Human T cells that may be used	according to these assays may	be isolated using techniques disclosed herein or otherwise	known in the art. Human T	lymphocytes that mature in the	thymus and express a T Cell	receptor and CD3, CD4, or	CD8. These cells mediate tumoral or cell-mediated	immunity and may be	preactivated to enhance	responsiveness to	immunomodulatory factors.
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and tissues, hemophilia, hypercoagulation, diabetes	mellitus, endocarditis, meningitis, Lyme Disease,	asthma and allergy.																											
			RANTES FMAT. Assays for	immunomodulatory proteins	that induce chemotaxis of T	cells, monocytes, and	eosinophils are well known in	the art and may be used or	routinely modified to assess the	ability of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to mediate	immunomodulation, induce	chemotaxis, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for immunomodulatory	proteins evaluate the production	of cytokines, such as RANTES,	and the induction of chemotactic	responses in immune cells.	Such assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays
			Production of	RANTES in	endothelial cells	(such as human	umbilical vein	endothelial cells	(HUVEC))	·																			
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			HAGEG10																										
				13																									

	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders").
disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which are endothelial cells (thute of that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may
	Activation of transcription through GAS response element in immune cells (such as T-
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ications	nd cance	, leukem	ell	S	lgkins	"s diseas	tate, brea	tic,	ı, brain,	icer. Oth	include	ive	oplastic	for exam	ısia, and/	pa.	utoimm	natoid	snd	ple scler	below),	(e.g., as	oosting a	ne respoi	cell-	sponse.	indicati	n and	lers.	lications	lers (e.g.	ler "Imm
erred ind	olasms a	example	e.g., T c	Burkitt'	non-Hoc	Hodgkir	and pros	pancrea	stomach	inary car	dications	roliferat	id pre-ne	such as,	, metapla	Preferred	include a	g., rheun	stemic lu	sis, multi	scribed	iciencies	elow), ba	ed immu	sing a T	ımune re	preferred	ammatio	ry disorc	erred inc	od disorc	elow une
Highly preferred indications	include neoplasms and cancers,	such as, for example, leukemia,	lymphoma (e.g., T cell	lymphoma, Burkitt's	lymphoma, non-Hodgkins	lymphoma, Hodgkin"s disease),	melanoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia.	indications include autoimmune	diseases (e.g., rheumatoid	arthritis, systemic lupus	erythematosis, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune response,	and suppressing a T cell-	mediated immune response.	Additional preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g., as	described below under "Immune
		ns	ly.	<u></u>	<u>-</u>	- <u> </u>	<u>u</u>	In	es —		bre	þe	di:		h	d _y	. <u>Ĕ</u>	Ğ	ar	er.	an	.⊑	g	3	an	Ĕ	Ă	<u> </u>	Ξ.			
be used or routinely modified to		vention	and	s of the	STAT	pu	sion	iety of	olary	assays for transcription through	the GAS response element that	ely	modified to test GAS-response	element activity of polypeptides	ding	ts or	ention)	ed in	:1-10	alm,	Methods in Enzymol 216:362-	et al.,	SA		po	9); and	lounu	155(10):4582-4587 (1995), the	hich are	herein incorporated by reference	olary	mouse T cells that may be used
utinely m	lity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate STAT	transcription factors and	modulate gene expression	involved in a wide variety of	cell functions. Exemplary	nscriptio	onse eler	may be used or routinely	est GAS.	ity of po	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	lomyzn	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	:-4587 (1	contents of each of which are	orated by	in its entirety. Exemplary	s that ma
ed or rou	assess the ability of	eptides	ıding anı	ists or an	tion) to	cription	ılate gen	ved in a	unctions	s for tra	AS resp	pe nsed	fied to te	ent activ	inventi	odies an	onists of	de assay	er et al.,	3); Culle	ods in E	(1992); F	Natl Ac	342-634	kainen e	1:1980-1	tinen et	10):4582	ents of ea	n incorp	entirety	se T cell
be us	asses	polyp	(inch	agoni	inven	transe	mode	invol	cell f	assay	the G	may	modi	elem	ofthe	antib	antag	inclu	Berg	(199	Meth	368 (Proc	85:6	Mati	93(6)	Hent	155(conte	herei	in its	mom
cells).																																
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				according to these assays are	Activity". "Blood-Related
_				publicly available (e.g., through	Disorders", and/or
				the ATCC). Exemplary T cells	"Cardiovascular Disorders"),
	-			that may be used according to	and infection (e.g., viral
				these assays include the CTLL	infections, tuberculosis,
		•		cell line, which is a suspension	infections associated with
				culture of IL-2 dependent	chronic granulomatosus disease
				cytotoxic T cells.	and malignant osteoporosis,
	_			•	and/or an infectious disease as
					described below under
			-		"Infectious Disease"). An
					additional preferred indication is
					idiopathic pulmonary fibrosis.
					Preferred indications include
					anemia, pancytopenia,
			•		leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas, multiple
					myeloma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted organs
					and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HAGES57	429	Activation of T-Cell	Kinase assay. JNK and p38	Preferred indications include
15		į	p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as

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described below under "Hynernroliferative Disorders").	, as	described below under "Immune	scular	3lood-	and	ections	pelow	sease").	ications	diseases	hritis,	ematosis,	d/or as	· C3	(e.g., as	dditional	cations	n and	inflammatory disorders. Highly	s also	include neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	ler	"Hyperproliferative Disorders").	lications	include neoplasms and cancers,	ymphoma,	3, colon,	pancreatic, esophageal, stomach,	brain, liver, and urinary cancer.	cations
described below under "Hynernoliferative Di	blood disorders (e.g., as	below und	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), and	infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	tory disord	preferred indications also	eoplastic d	, lymphom	described below under	oliferative	Highly preferred indications	eoplasms a	such as, leukemia, lymphoma,	prostate, breast, lung, colon,	c, esophage	er, and urir	Other preferred indications
described "Hynernic	blood disc	described	Activity",	Disorders	Related D	infection (disease as	under "Inf	Highly pr	include au	(e.g., rheu	systemic	multiple s	described	immunod	described	highly pre	include in	inflamma	preferred	include ne	leukemia,	described	"Hyperpr	Highly pr	include n	such as, l	prostate,	pancreati	brain, live	Other pre
e cell	n in the	outinely	bility of	ntion	р	of the	r inhibit		, and	ssays for	ivity that	×	d p38	of	ntion	- Pi	of the	ssays	"Biol	110	p Cell	999);	Soc	Chang); and	/s Mol	1999);	which	by	Teells
hat regulat	well know	e used or r	ssess the al	of the inve	tibodies an	tagonists (promote or	e.g. T-cell	activation	cemplary a	kinase act	or routinel	est JNK an	ed activity	of the inve	tibodies ar	ntagonists (clude the a	orrer et al	9):1101-1	a et al., Ex	195-504 (1)	Biochem	48 (1999);	ature	7-40 (2001	rog Biophy	479-500 (of each of	corporated	ts entirety
transduction that regulate cell	apoptosis are well known in the	art and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to promote or inhibit	immune cell (e.g. T-cell)	proliferation, activation, and	apoptosis. Exemplary assays for	JNK and p38 kinase activity that	may be used or routinely	modified to test JNK and p38	kinase-induced activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Gupta et al., Exp Cell	Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety. T cells
tra	produce and approved the produce of	art	m	0	Ü.	age		<u> </u>	pre	ab	<u>Z</u>	Ë	Ĕ	Ķ.	<u></u>	.E	aga	. <u>:</u>	dis	<u>ਹ</u>		<u>~</u>	×	S	an,	41	<u>ပ</u>	B	\$	ar	
Pathway.																															
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include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatory bowel disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as
that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for
	Production of IL-6
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		immunomodulatory and	described below under "Immune
		differentiation factor proteins	Activity", "Blood-Related
		produced by a large variety of	Disorders", and/or
		cells where the expression level	"Cardiovascular Disorders"),
		is strongly regulated by	and infection (e.g., as described
		cytokines, growth factors, and	below under "Infectious
		hormones are well known in the	Disease"). Highly preferred
		art and may be used or routinely	indications include autoimmune
 		modified to assess the ability of	diseases (e.g., rheumatoid
		polypeptides of the invention	arthritis, systemic lupus
		(including antibodies and	erythematosis, multiple sclerosis
		agonists or antagonists of the	and/or as described below) and
		invention) to mediate	immunodeficiencies (e.g., as
		immunomodulation and	described below). Highly
		differentiation and modulate T	preferred indications also
		cell proliferation and function.	include boosting a B cell-
		Exemplary assays that test for	mediated immune response and
		immunomodulatory proteins	alternatively suppressing a B
		evaluate the production of	cell-mediated immune response.
 •		cytokines, such as IL-6, and the	Highly preferred indications
		stimulation and upregulation of	include inflammation and
	•	T cell proliferation and	inflammatory
		functional activities. Such	disorders.Additional highly
		assays that may be used or	preferred indications include
		routinely modified to test	asthma and allergy. Highly
		immunomodulatory and	preferred indications include
		diffferentiation activity of	neoplastic diseases (e.g.,
		polypeptides of the invention	myeloma, plasmacytoma,
		(including antibodies and	leukemia, lymphoma,
		agonists or antagonists of the	melanoma, and/or as described
		invention) include assays	below under "Hyperproliferative
		disclosed in Miraglia et al., J	Disorders"). Highly preferred
		Biomolecular Screening 4:193-	indications include neoplasms

and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer.	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, bynercoagulation, diahetes	mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of	Which are never in the opporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in	activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	

Se A Se 7 e 3	 IL-10 Highly preferred indications are include allergy and asthma. I may Additional highly preferred indications include immune and
Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to
	Production of IL-10 and activation of T-cells.
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hematopoietic disorders (e.g., as	described below under "Immune	Activity", and "Blood-Related	Disorders"), autoimmune	diseases (e.g., rheumatoid	arthritis, systemic lupus	erythematosis, Crohn's disease,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune response,	and suppressing a T cell-	mediated immune response.	-																		
assess the ability of	nolypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate or inhibit	production of IL-10 and/or	activation of T-cells.	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including agonists	or antagonists of the invention)	to modulate IL-10 production	and/or T-cell proliferation	include, for example, assays	such as disclosed and/or cited	in: Robinson, DS, et al., "Th-2	cytokines in allergic disease" Br	Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the contents	of each of which are herein	incorporated by reference in	their entirety. Exemplary cells	that may be used according to	these assays include Th2 cells.	IL10 secreted from Th2 cells	may be measured as a marker of	Th2 cell activation. Th2 cells
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		A highly preferred embodiment of the invention includes a method for inhibiting
such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "Thelper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete 1L4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using	isolated from cord blood.	TNFa FMAT. Assays for immunomodulatory proteins produced by activated
		Production of TNF alpha by dendritic cells
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(e.g., decreasing) TNF alpha	production. An alternative	highly preferred embodiment of	the invention includes a method	for stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,
macrophages, T cells,	fibroblasts, smooth muscle, and	other cell types that exert a wide	variety of inflammatory and	cytotoxic effects on a variety of	cells are well known in the art	and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, modulate	inflammation and cytotoxicity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or cytotoxic	response. Such assays that may	be used or routinely modified to	test immunomodulatory activity	of polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160
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leukemia, lymphoma, and/or as described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophilia,	psoriasis, suppression of	immune reactions to	transplanted organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocatutus,
(2000); Verhasselt et al., Eur J	(1198); Dahlen et al., J Immunol	160(7):3585-3593 (1998);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells	that may be used according to	these assays may be isolated	using techniques disclosed	herein or otherwise known in	the art. Human dendritic cells	are antigen presenting cells in	suspension culture, which, when	activated by antigen and/or	cytokines, initiate and	upregulate T cell proliferation	and functional activities.									•		
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acturiac reperfusion injury, and additional preferred indication is infectious disease as described below transcription through the EGR (Early Growth Response) activity of polypeptides of the invention include using transcription through the EGR (movement in immune used or routinely modified to antipodres, agonists, or cells, cucl as B- polypeptides of the invention include using transcription through the EGR (movement in the art and may be element in immune used or routinely modified to antipodres, agonists, or cells). (including antibodies and agonists of the invention of carrows are polypeptides of the invention of carrows are consistent that may be used or routinely modified to reasonable and agonists of the invention factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely modified to test EGR response element that may be used or routinely of polypeptides of the invention) include assays disclosed in Richards Dt, et al., EGR assays that all assays that all assays that all assays that all a	ļ					meningitis, Lyme Disease,
Activation of transcription through the EGR transcription through tresponse element are well-Growth Response) known in the art and may be element in immune used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate EGR transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element that may be used or routinely modified to test EGR response element activity of polypeptides of the invention) include assays disclosed in: Richards JD, et al., J Exp J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp						cardiac reperfusion injury, and
433 Activation of transcription through the EGR transcription in the art and may be element in immune used or routinely modified to assess the ability of cells. Cells. Cells. Colls. Colls. Colls. Exemplary assays for the invention (including antibodies and agonists or antagonists of the invention) to regulate EGR transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Exp J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp		-				asthma and allergy. An
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response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate EGR transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element that may be used or routinely modified to test EGR response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp		/FOOGH		transcription through	transcription through the EGR	invention include using
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(including antibodies and agonists or antagonists of the invention) to regulate EGR transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element that may be used or routinely modified to test EGR response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp				cells).	polypeptides of the invention	treatment of Cancer,
R. S. S. S. S. A. S.				`	(including antibodies and	Autoimmunity, Allergy and
invention) to regulate EGR transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element that may be used or routinely modified to test EGR response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp					agonists or antagonists of the	Asthma.
transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element that may be used or routinely modified to test EGR response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp					invention) to regulate EGR	
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activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp					test EGR response element	
invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp					activity of polypeptides of the	· inc
and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp			-		invention (including antibodies	
the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp					and agonists or antagonists of	
disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp					the invention) include assays	
J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp					disclosed in: Richards JD, et al.,	
(2001); Dinkel, A, et al., J Exp					J Immunol, 166(6):3855-3864	
					(2001); Dinkel, A, et al., J Exp	

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Infection, Cancer, Hypersensitivity, and Atherosclerosis.
Med, 188(12):2215-2224 (1998); and, Newton, JS, et al., Eur J Immunol 1996 Apr;26(4):811-816 (1996), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the Raji cell line.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely
	Activation of transcription through GAS response element in immune cells (such as monocytes).
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modified to test GAS-response	element activity of polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in:	Gustafson KS, et al., J Biol	Chem, 271(33):20035-20046	(1996); Eilers A, et al.,	Immunobiology, 193(2-4):328-	333 (1995); Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by reference	in its entirety. Exemplary	immune cells that may be used	according to these assays are	publicly available (e.g., through	the ATCC). Exemplary immune	cells that may be used according	to these assays include the U937	cell line, which is a monocytic	cell line.	Kinase assay. Kinase assays,
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Signaling Pathway assay, for ERK signal includes a method for
proliferation or differentiation
proliferation of differentiallor are well known in the art and
are well known in the art and may be used or routinely
are well known in the art and may be used or routinely modified to assess the ability

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and/or as described below under "Hyperproliferative Disorders").	Preferred indications include	blood disorders (e.g.,	hypertension, congestive heart	failure, blood vessel blockage,	heart disease, stroke, impotence	and/or as described below under			and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	_	below under "Infectious	Disease"). A highly	preferred indication is diabetes	mellitus. An additional	highly preferred indication is a	complication associated with	diabetes (e.g., diabetic	retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure, nephropathy	and/or other diseases and	disorders as described in the	"Renal Disorders" section	below), diabetic neuropathy,	nerve disease and nerve damage
are herein incorporated by reference in its entirety. Mouse	adipocyte cells that may be used	according to these assays are	publicly available (e.g., through	the ATCC). Exemplary mouse	adjpocyte cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1 is	an adherent mouse preadipocyte	cell line that is a continuous	substrain of 3T3 fibroblast cells	developed through clonal	isolation and undergo a pre-	adinocyte to adipose-like	conversion under appropriate	differentiation conditions known	in the art															
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(e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic nauropathy or blood vessel	blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the	below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious	Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred

indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin	resistance. Additional highly preferred indications are disorders of the musculoskeletal	systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications	artery disease, dyslipidemia,	degenerative arthritis, eating disorders, fibrosis, cachexia, and	Preferred indications include neoplasms and cancer, such as,	lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications	include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and	indications include lipomas and liposarcomas. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,
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					metaplasia, and/or dysplasia.
	HAOAG15	435	Activation of	Kinase assay. Kinase assays,	A highly preferred
21			Natural Killer Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
			Pathway.	transduction that regulate cell	stimulating natural killer cell
			•	proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment of
				may be used or routinely	the invention includes a method
				modified to assess the ability of	for inhibiting natural killer cell
				polypeptides of the invention	proliferation. A highly
				(including antibodies and	preferred embodiment of the
			,	agonists or antagonists of the	invention includes a method for
				invention) to promote or inhibit	stimulating natural killer cell
				cell proliferation, activation, and	differentiation. An alternative
				differentiation. Exemplary	highly preferred embodiment of
				assays for ERK kinase activity	the invention includes a method
				that may be used or routinely	for inhibiting natural killer cell
				modified to test ERK kinase-	differentiation. Highly
				induced activity of polypeptides	preferred indications include
				of the invention (including	neoplastic diseases (e.g., as
				antibodies and agonists or	described below under
				antagonists of the invention)	"Hyperproliferative Disorders"),
				include the assays disclosed in	blood disorders (e.g., as
				Forrer et al., Biol Chem 379(8-	described below under "Immune
				9):1101-1110 (1998); Kyriakis	Activity", "Cardiovascular
				JM, Biochem Soc Symp 64:29-	Disorders", and/or "Blood-
				48 (1999); Chang and Karin,	Related Disorders"), immune
				Nature 410(6824):37-40 (2001);	disorders (e.g., as described
				and Cobb MH, Prog Biophys	below under "Immune
				Mol Biol 71(3-4):479-500	Activity") and infections (e.g.,
				(1999); the contents of each of	as described below under
				which are herein incorporated	"Infectious Disease").

Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders" and/or	"Cardiovascular Disorders"). Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,	described below) and immunodeficiencies (e.g., as described below). Additional	highly preferred indications include inflammation and inflammation.	Highly preferred indications also include cancers such as,	kidney, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver, urinary cancer, lymphoma and leukemias. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred	indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease,
by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g.,	through the ATCC). Exemplary natural killer cells that may be used according to these assays	include the human natural killer cell lines (for example, NK-YT cells which have cytolytic and	cytotoxic activity) of priniary NK cells.							
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acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
	Kinase assays, for example an Elk-1 kinase assay for ERK signal transduction that regulates cell proliferation or differentiation, are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Ali H, et al., J Immunol, 165(12):7215-7223
	Regulation of proliferation and/or differentiation in immune cells (such as mast cells).
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	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as
(2000); Tam SY, et al., Blood, 90(5):1807-1820 (1997); Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Berra et al., Biochem Pharmacol 60(8):1171-1178 (2000); Gupta et al., Exp Cell Res 247(2):495-504 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells that may be used according to these assays include human mast cells such as the HMC-1 cell line.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of
	Production of IL-10 and activation of T-cells.
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described below), boosting a T cell-mediated immune response,	and suppressing a T cell-	mediated immune response.																													
polypeptides and antibodies of	or antagonists of the invention)	to modulate IL-10 production	and/or T-cell proliferation	include, for example, assays	such as disclosed and/or cited	in: Robinson, DS, et al., "Th-2	cytokines in allergic disease" Br	Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the contents	of each of which are herein	incorporated by reference in	their entirety. Exemplary cells	that may be used according to	these assays include Th2 cells.	IL10 secreted from Th2 cells	may be measured as a marker of	Th2 cell activation. Th2 cells	are a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation of	Th2 cells play a major role in	the initiation and pathogenesis	of allergy and asthma. Primary	Thelper 2 cells are generated	via in vitro culture under Th2	polarizing conditions using
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eins ast in ophils (Ils into in the outinely illity of intion and in and/or emplary of and the ill and the stans of and the ill stans of state state in stans of and the ill stans of state stans of and the ill					peripheral blood lymphocytes isolated from cord blood.	
immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil function and B cell lg production and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polyoptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cell function, modulate immune cell function, modulate B cell Ig production, modulate be colling production, modulate immune cell function proteins evaluate the production of ecytokines, such as IL-5, and the stimulation of eosinophil function and B cell Ig production. Such assays that tender may be used or routinely modifical to test or routinely may be used or routinely modulation.		HAOCEII	438	Production of IL-5	IL-5 FMAT. Assays for	A highly preferred
secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil function and B cell Ig production and B cell Ig production and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immuno cell function, modulate immuno cell polarization, and/or mediate humoral or cell-mediate humoral or cell-immunomodulatory proteins evaluate the production of cytokines, such as IL-5, and the stimulation of eosinophil function and B cell Ig production. Such assays that may be used or routinely	24	, , , , , , , , , , , , , , , , , , ,) }		immunomodulatory proteins	embodiment of the invention
Ils into Ils into In in the outinely sility of ntion d of the odulate odulate odulate in, and/or teins of and the il	† 7	2			secreted by TH2 cells, mast	includes a method for inhibiting
Ils into n in the outinely sility of ntion d of nulate nodulate odulate in, and/or teins of and the il					cells, basophils, and eosinophils	(e.g., reducing) IL-5 production.
te cells into own in the r routinely ability of vention and s of the inmulate modulate modulate modulate conto fell-Exemplary of 5, and the phil	-		-		that stimulate eosinophil	An alternative highly preferred
cells into own in the r routinely ability of vention and s of the finulate modulate ion, and/or ell- Exemplary rroteins on of -5, and the phil					function and B cell Ig	embodiment of the invention
					production and promote	includes a method for
L					polarization of CD4+ cells into	stimulating (e.g., increasing)
L					TH2 cells are well known in the	IL-5 production. A highly
<u>.</u>	_				art and may be used or routinely	preferred embodiment of the
<u> </u>					modified to assess the ability of	invention includes a method for
the ulate dulate unlate and/or mplary fr ind the that					polypeptides of the invention	stimulating (e.g., increasing)
the and					(including antibodies and	immunoglobulin production. An
ary					agonists or antagonists of the	alternative highly preferred
itimulate i, modulate modulate iion, and/or ell- Exemplary oroteins on of -5, and the phil					invention) to mediate	embodiment of the invention
or ry or le					immunomodulation, stimulate	includes a method for inhibiting
dulate i, and/or implary eins of and the that	_				immune cell function, modulate	(e.g., decreasing)
and/or sins of and the that					B cell Ig production, modulate	immunoglobulin production.
eins of the that					immune cell polarization, and/or	A highly preferred indication
eins of the that					mediate humoral or cell-	includes allergy. A highly
					mediated immunity. Exemplary	preferred indication includes
					assays that test for	asthma. A highly preferred
					immunomodulatory proteins	indication includes rhinitis.
				-	evaluate the production of	An additional highly preferred
					cytokines, such as IL-5, and the	indication is infection (e.g., an
ys that		-			stimulation of eosinophil	infections disease as described
ys that					function and B cell Ig	below under "Infectious
<u> </u>				•	production. Such assays that	Disease"), and inflammation and
modified to feet				-	may be used or routinely	inflammatory disorders.
ווווחוווו וווחוווו					modified to test	Preferred indications include

blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic		nelanoma, 19mphonia, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, and	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias,
immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al.,	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Ohshima et al., Blood 92(9):338-3345 (1998); Jung et al., Eur J Immunol 25(8):2413-2416 (1995); Mori et al., J	Allergy Clin Immunol 106(1 Pt 2):558-564 (2000); and Koning et al., Cytokine 9(6):427-436 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used	according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance

Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
responsiveness to immunomodulatory factors.	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as
	Production of MIP1alpha
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Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs		hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under
macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of	monocytes/macrophages and T	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and Eremin,	J R Coll Surg Ednb 45(1):9-19	(2001); Drakes et al., Transp	Immunol 8(1):17-29 (2000);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells	that may be used according to	these assays may be isolated	using techniques disclosed	herein or otherwise known in	the art. Human dendritic cells
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"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A nignly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins
	Production of TNF alpha by dendritic cells
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	HATB194
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Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").		indications include neoplasms	and cancers, such as, leukemia,	Iymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,
evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or cytotoxic	response. Such assays that may	be used or routinely modified to	test immunomodulatory activity	of polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J Immunol	160(7):3585-3593 (1998);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells	that may be used according to	these assays may be isolated	using techniques disclosed	herein or otherwise known in	the art. Human dendritic cells
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hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic	anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,	neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,	hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,	cardiac repertusion injury, and asthma and allergy. An additional preferred indication is	infection (e.g., an infectious disease as described below under "Infectious Disease").				A highly preferred embodiment of the invention
are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.									Kinase assay. Kinase assays, for example an GSK-3 kinase
						CD152 in Human T cells	VEGF in HT1080	CD69 in Human T cells	Activation of Skeletal Mucle Cell
						440	441	441	441
						HATCB45	HATC103	HATCI03	HATCI03
						36	7.2	7.7	27

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		indications include disorders of
Pl3 Kinase Signalling Pathway	glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the	myoblast cells that may be used
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the musculoskeletal system. Preferred indications include line, neoplastic diseases (e.g., as described below under uses to "Hyperproliferative Disorders"), tubes endocrine disorders (e.g., as		Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is	diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy,
according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes	in differentiation media.		

nerve disease and nerve damage	(e.g, due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, infections (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract	and skin), carpal tunnel	syndrome and Dupuytren's	contracture). An additional	highly preferred indication is
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obesity and/or complications associated with obesity. Additional highly preferred	indications include weight loss or alternatively, weight gain. Additional highly preferred	indications are complications associated with insulin resistance. Additonal	highly preferred indications are disorders of the musculoskeletal	system including myopathies, muscular dystrophy, and/or as	described herein. Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and vascular disease. Highly preferred	indications include neoplasms	and cancer, such as,	rhabdomyoma, rhabdosarcoma,	stomach, esophageal, prostate,	and urinary cancer. Preferred	indications also include breast,	lung, colon, pancreatic, brain,	and liver cancer. Other	preferred indications include	benign dysproliterative
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disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.		A preferred embodiment of	the invention includes a method	for inhibiting (e.g., reducing)	TNF alpha production. An	alternative highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Preferred indications include	blood disorders (e.g., as	described below under "Immune			_	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional
		Assays for the activation of	transcription through the Serum	Response Element (SRE) are	well-known in the art and may	be used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate serum	response factors and modulate	the expression of genes involved	in growth and upregulate the	function of growth-related genes	in many cell types. Exemplary	assays for transcription through	the SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,
	SEAP in HIB/CRE	Activation of	transcription through	serum response	element in immune	cells (such as natural	killer cells).	`																				
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highly preferred indications	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,
Proc Natl Acad Sci USA	al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary T cells that	may be used according to these	assays include the NK-YT cell	line, which is a human natural	killer cell line with cytolytic and	cytotoxic activity.																
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multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred indication is diabetes mellitus. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel
	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The
	Regulation of transcription via DMEF1 response element in adipocytes and preadipocytes
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blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental	confusion, drowsiness, nonketotic hyperglycemic-			described in the "Cardiovascular Disorders" section below),	dyslipidemia, endocrine disorders (as described in the	"Endocrine Disorders" section	below), neuropatny, vision impairment (e.g., diabetic	retinopathy and blindness), ulcers and impaired wound	healing, and infection (e.g., infections diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract and skin). An additional highly	preferred indication is obesity	and/or complications associated	with obesity. Additional nighty preferred indications include	weight loss or alternatively,	weight gain. Additional highly
present in the GLUT4 promoter and binds to MEF2 transcription	factor that is required for insulin regulation of Glut4 expression	the primary insulin-responsive glucose transporter in fat and	muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1	response element activity (in adipocytes and pre-adipocytes)	by polypeptides of the invention (including antibodies and	agonists or antagonists of the	invention) include assays disclosed in Thai, M.V., et al., J	Biol Chem, 273(23):14285-92 (1998): Mora. S., et al., J Biol	Chem, 275(21):16323-8 (2000);	269(45):28514-21 (1994);	"Identification of a 30-base pair	regulatory element and novel	regulates the human GLUT4	promoter in transgenic mice", J	Biol Chem. 2000 Aug	al., Gene 66:1-10 (1988); and,	Cullen, B., et al., Methods in
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preferred indications are complications associated with insulin resistance.		A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred
Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.		Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the
	SEAP in 3T3L1	Activation of transcription through cAMP response element (CRE) in pre-adipocytes.
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healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic
which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved
	Activation of transcription through serum response element in preadipocytes.
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nephropathy, kidney disease	(e.g., renal failure, nephropathy	and/or other diseases and	disorders as described in the	"Renal Disorders" section	below), diabetic neuropathy,	nerve disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g.,	infectious diseases and disorders	as described in the "Intectious
in growth Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998): Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and Black	et al., Virus Genes 12(2):105-	117 (1997), the content of each	of which are herein incorporated	by reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g., through	the ATCC) and/or may be	routinely generated. Exemplary	mouse adipocyte cells that may	be used according to these	assays include 3T3-L1 cells.	3T3-L1 is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to
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Diseases" section below). Additional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,
adipose-like conversion under appropriate differentiation conditions known in the art.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely modified to test GATA3-response element activity of
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
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liver, and urinary tract cancers and/or as described below under	"Hyperproliferative Disorders). Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,		reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.				-				
polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assavs	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell et	al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur J	Immunol 29(12):3914-3924	(1999); Zheng and Flavell, Cell	89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by reference	in its entirety. Mast cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-1	cell line, which is an immature	human mast cell line established	from the peripheral blood of a	patient with mast cell leukemia,	and exhibits many	characteristics of immature mast
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			cells.		
TID A CID 86	443	Activation of	This reporter assay measures	Highly preferred indications	
HBACDeo	Ct t	transcription through	activation of the NFAT	include allergy, asthma, and	
		NFAT response	signaling pathway in HMC-1	rhinitis. Additional preferred	
		element in immine	human mast cell line. Activation	indications include infection	
		cells (such as mast	of NFAT in mast cells has been	(e.g., an infectious disease as	
		cells)	linked to cytokine and	described below under	
		cons).	chemokine production. Assays	"Infectious Disease"), and	
			for the activation of	inflammation and inflammatory	
			transcription through the	disorders. Preferred indications	
			Nuclear Factor of Activated T	also include blood disorders	
			cells (NFAT) response element	(e.g., as described below under	
			are well-known in the art and	"Immune Activity", "Blood-	
			may be used or routinely	Related Disorders", and/or	
-			modified to assess the ability of	"Cardiovascular Disorders").	
			nolvoeptides of the invention	Preferred indications include	
			(including antibodies and	autoimmune diseases (e.g.,	
			agonists or antagonists of the	rheumatoid arthritis, systemic	
			invention) to regulate NFAT	lupus erythematosis, multiple	
			transcription factors and	sclerosis and/or as described	
			modulate expression of genes	below) and immunodeficiencies	
			involved in immunomodulatory	(e.g., as described below).	
		-	functions. Exemplary assays for	Preferred indications include	
	_		transcription through the NFAT	neoplastic diseases (e.g.,	
			response element that may be	leukemia, lymphoma,	
			used or routinely modified to	melanoma, prostate, breast,	
		-	test NFAT-response element	lung, colon, pancreatic,	
			activity of polypeptides of the	esophageal, stomach, brain,	
		-	invention (including antibodies	liver, and urinary tract cancers	
			and agonists or antagonists of	and/or as described below under	
			the invention) include assays	"Hyperproliferative Disorders").	
			disclosed in Berger et al Gene	Other preferred indications	_

include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many	This reporter assay measures activation of the NFkB signaling pathway in HMC-1 human mast
027000000000000000000000000000000000000	Activation of transcription through NFKB response
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element in immune cells (such as mast cells).	KB KB Co. 10 Line St. 11 Line St. 12 Line	preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g., as described below under "Hondre autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast,
	Maim, Methods III Enzymor 216:362-368 (1992); Henthorn	lung, colon, pancreatic,
	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Stassen et	esophageal, stomach, brain, liver, urinary tract cancers and
 	al, J Immunol 166(7):4391-8	as described below under

"Hyperproliterative Disorders".	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g., as described below under "Immune Activity", and
Walker, J Allergy Clin Immunol 105(3):500-5 (2000), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB
·	Activation of transcription through NFKB response element in immune cells (such as basophils).
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	HBAGD86
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"Blood-Related Disorders"). Preferred indications also	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative Disorders".	-								
transcription factors and modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the NFKB	response element that may be	used or rountinely modified to	test NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm. Methods in Enzymol	216:362-368 (1992); Henthorn	et al Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone et	al, Int Arch Allergy Immunol	114(3):207-17 (1997), the	contents of each of which are	herein incorporated by reference	in its entirety. Basophils that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary human basophil cell	lines that may be used according	to these assays include Ku812,	originally established from a	patient with chronic	myelogenous leukemia. It is an	immature prebasophilic cell line
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			that can be induced to differentiate into mature basonhils.	
HBAGD86	443	SEAP in Molt4/SRE		
HBAGD86	443	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred inflammation and inflammatory disorders. An additional highly preferred inflectious disease as described below under "Infectious Disease"). Preferred indications include neonlastic diseases (e.g.,

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leukemia, lymphoma, and/or as described below under	"Hyperproliferative Disorders").	Preferred indications include	neoplasms and cancers, such as,	for example, leukemia,	lymphoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic			dysplasia. Preferred	indications also include anemia,			disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,
et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	Aramburu et al., J Exp Med	182(3):801-810 (1995); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Veseen et al., J Biol Chem	268(19)-14285-14293 (1993).	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used according	to these assays are publicly	weilable (e.g. through the	ATCC Exemplary human NK	cells that may be used according	to these assays include the NK-	VT cell line, which is a human	natural killer cell line with	cytolytic and cytotoxic activity.											
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T.:: 20 * T.:: 82 - 1 - 1 - 2						asthma and allergy.
HBAGD86 443 SEAP in OE-21 HBAGD86 443 transcription through the transcription through the transcription through the GAS response cells (such as T-cells (such as T-cells). Ells) assess the ability of polypeptides of the invention of (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and may be used or routinely modified to ell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element that may be used or routinely modified to test GAS-response element that may be used or routinely modified to test GAS-response element and Malm. (1998); Cullen and Malm. Heads of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm. Methods in Elazymol 21 (6:362-		HBAGD86	443	SEAP in		
HBAGD86 443 Activation of transcription through the GAS response element in immune Site (GAS) response element are cells (such as T-cells). Cells, well-known in the art and may evel-known in the art and may onlypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) including antibodies and agonists or the invention) including antibodies and agonists or antagonists of the invention) including antibodies and agonists or antagonists of the invention) including antibodies and agonists or antagonists of the invention) (1998); Cullen and Malm. (1998); Cullen and Malm. (1998); Cullen and Malm. (1998); Cullen and Malm. (1998); Cullen and Malm.	59	HBAGD86	443	SEAP in OE-21		
HBAGD86 Hanscription through transcription through the Garman Interferon Activation Element in immune dement in immune cells (such as Tells (Such as Tells). Site (GAS) response element are cells, et al. From in the art and may be used or routinely modified to polypeptides of the invention of including antibodies and agonists or antagonists of the invention of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test CAS-response element activity of polypeptides of the invention) including antibodies and agonists or antagonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm. Methods in Enzymol 216:362-	29			J	A seave for the activation of	Highly preferred indications
Gamma Interferon Activation GAS response cells (such as T- cells). Site (GAS) response element are well-known in the art and may cells). assess the ability of assess the ability of including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm. Methods in Enzymol 216:362-		HBAGD86	443	Activation of	ranscription through the	include neoplastic diseases (e.g.,
Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	29			GAS response	Gamma Interferon Activation	leukemia, lymphoma, and/or as
such as T- be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-				element in immune	Site (GAS) response element are	described below under
be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-				cells (such as T-	well-known in the art and may	"Hyperproliferative Disorders").
assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-				cells)	be used or routinely modified to	Highly preferred indications
s and sts of the te STAT and ession ariety of mplary ion through lement that inely .S-response polypeptides cluding nists or nvention) losed in 66:1-10 Malm,				.(2113).	assess the ability of	include neoplasms and cancers,
gh at se des con 2-					polypeptides of the invention	such as, for example, leukemia,
gh at see des 2-			•		(including antibodies and	lymphoma (e.g., T cell
gh at see des des 2-					agonists or antagonists of the	lymphoma, Burkitt's
ty of ry chrough chrough sint that y sponse peptides ing or tion) 1 in 1 in 1 in 2.10 m,					invention) to regulate STAT	lymphoma, non-Hodgkins
ty of rry hrough ant that y sponse peptides ing or tion) 1 in					transcription factors and	lymphoma, Hodgkin"s disease),
gh at see des des 2-					modulate gene expression	melanoma, and prostate, breast,
gh at see des des 2-					involved in a wide variety of	lung, colon, pancreatic,
that that onse ptides ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' '					cell functions. Exemplary	esophageal, stomach, brain,
					assays for transcription through	liver and urinary cancer. Other
S		-			the GAS response element that	preferred indications include
ponse eptides lg r r c on) in lin lin lin lin lin lin lin lin lin	. 				may be used or routinely	benign dysproliferative
					modified to test GAS-response	disorders and pre-neoplastic
			,		element activity of polypeptides	conditions, such as, for example,
n))) 862-	,				of the invention (including	hyperplasia, metaplasia, and/or
2-					antibodies and agonists or	dysplasia. Preferred indications
2-					antagonists of the invention)	include autoimmune diseases
62-		-	-1-		include assays disclosed in	(e.g., rheumatoid arthritis,
				4	Berger et al., Gene 66:1-10	systemic lupus erythematosis,
					(1998); Cullen and Malm,	multiple sclerosis and/or as
					Methods in Enzymol 216:362-	described below),

immunodeficiencies (e.g., as described below), boosting a T	cell-mediated immune response,	and suppressing a T cell-	mediated immune response.	Additional preferred indications	inflammatory disorders. Highly			described below under "Immune	Activity", "Blood-Related		"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus disease	and malignant osteoporosis,	and/or an infectious disease as	described below under	"Infectious Disease"). An	additional preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas, multiple	myeloma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,
368 (1992); Henthorn et al.,	Fig. 1342 85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	berein incorporated by reference	in its entirety. Exemplary	himan T cells, such as the	SUPT cell line, that may be used	seconding to these assays are	according to the control with a sailable (e.g., through	the ATCC)	inc at co):																	
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neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease, and	asthma and allergy.	A highly preferred embodiment	of the invention includes a	method for stimulating (e.g.,	increasing) IL-6 production. An	alternative highly preferred	embodiment of the invention	includes a method for inhibiting	(e.g., reducing) IL-6 production.	A highly preferrred indication is	the stimulation or enhancement	of mucosal immunity. Highly	preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as described	below under "Infectious			_	arthritis, systemic lupus	erythematosis, multiple sclerosis
								II -6 FMAT. IL-6 is produced	by T cells and has strong effects	on B cells. IL-6 participates in	II4 induced IgE production	and increases IgA production	(IoA plays a role in mucosal	imminity). IL-6 induces	cytotoxic T cells. Deregulated	expression of IL-6 has been	linked to autoimmune disease,	plasmacytomas, myelomas, and	chronic hyperproliferative	diseases. Assays for	imminomodulatory and	differentiation factor proteins	produced by a large variety of	cells where the expression level	is strongly regulated by	cytokines, growth factors, and	hormones are well known in the	art and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and
								Description of II -6																							
									444						_							_				-			<u>-</u>	-	
									HBCJL33	30						_															

and/or as described below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response and	alternatively suppressing a B	cell-mediated immune response.	Highly preferred indications	include inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliterative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	Iymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or
anonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and the	stimulation and upregulation of	T cell proliferation and	functional activities. Such	assavs that may be used or	routinely modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using
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dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL),	lymphoma, arthritis, AIDS,	granulomatous disease, inflammatory bowel disease,	sepsis, neutropenia, neutrophilia, psoriasis,	suppression of immune reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.	An additonal preferred	indication is infection (e.g., an	infectious disease as described	below under "Intectious Disease").	A highly preferred	embodiment of the invention	includes a method for	Stifficiating chacterian con	preferred embodiment of the	invention includes a method for	inhibiting endothelial cell	embodiment of the invention
techniques disclosed herein or otherwise known in the art.	antigen presenting cells in suspension culture, which, when	activated by antigen and/or cytokines, initiate and	upregulate T cell proliferation and functional activities.										Caspase Apoptosis Rescue.	Assays for caspase apoptosis	rescue are well known in the art	and may be used or routinely	modified to assess the ability of the	invention (including antibodies	and agonists or antagonists of	the invention) to inhibit caspase protease-mediated apoptosis.
													Drotection from	Fudothelial Cell	Apoptosis.					
,													445	C 440						
														HBGBC29						
														,	31					

hypertrophy. An alternative highly preferred embodiment of the invention includes a method	for inducing cardiac hypertrophy. Highly	preferred indications include neonlastic diseases (e.g., as	described below under	"Hyperproliferative Disorders"), and disorders of the	cardiovascular system (e.g.,	heart disease, congestive heart	failure, hypertension, aortic	stenosis, cardiomyopathy,	valvular regurgitation, left	ventricular dysfunction,	atherosclerosis and	atherosclerotic vascular disease,	diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels such	as diabetes mellitus, as well as	diseases of the vessels	themselves, such as of the
			_																								

arteries, capillaries, veins and/or	lymphatics). Highly preferred	are indications that stimulate	angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors, leukemias,	and Kaposi"s sarcoma, and	retinal disorders. Highly	preferred indications include	neoplasms and cancer, such as,	Kaposi"s sarcoma, hemangioma	(capillary and cavernous),	glomus tumors, telangiectasia,	bacillary angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver, and urinary cancer.	Preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,
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hyperplasia, metaplasia, and/or dvsnlasia. Highly preferred	indications also include arterial	disease, such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's disease	and Reynaud"s phenomenom,	aneurysms, restenosis; venous	and lymphatic disorders such as	thrombophlebitis, lymphangitis,	and lymphedema; and other	vascular disorders such as	peripheral vascular disease, and	cancer. Highly preferred	Suc	such as wounds, burns, and	injured tissue (e.g., vascular	injury such as, injury resulting	from balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke, graft	rejection, diabetic or other	retinopathies, thrombotic and	coagulative disorders,	vascularitis, lymph
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				ally logeries is, sexual disolucis.
				age-related macular
				degeneration, and treatment
		and the second		/prevention of endometriosis
				and related conditions.
				Additional highly preferred
				indications include fibromas,
				heart disease, cardiac arrest,
				heart valve disease, and vascular
				disease. Preferred indications
				include blood disorders (e.g., as
				described below under "Immune
				Activity", "Blood-Related
				Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and immunodeficiencies
				(e.g., as described below).
				Additional preferred indications
				include inflammation and
	-	-		inflammatory disorders (such as
				acute and chronic inflammatory
				diseases, e.g., inflammatory
				bowel disease and Crohn's
		1.0		disease), and pain management.
HBGBC29 445 Inhibition of	445	Jo u	Reporter Assay: construct	
31 squalene synthetase	squalene	synthetase	contains regulatory and coding	
gene transcription.	gene trar	scription.	sequence of squalene	

herayment in the choisearcoi biogynthetic pathway. See Jiang, et al., 1. Biol. Chem. 268:12818-12824 (1933), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supermatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 200-4579-9 (1980), the contents of which are herein incorporated by reference in its entirety. Assays for production of IL-10 and activation of Te-8ls are well known in the art and may he used or routinely modified to hematopoietic disorders (e.g., as polypeptides of the invention functioning antibodies and assess the ability of production of IL-10 and/or activation of T-cells. Exemplary assays that may be invention) to stimulate or inhigh efferencies (e.g., as seemblary assays that may be inmunodefricencies (e.g., as inmunodefricencies (e.g., as

cell-mediated immune response, and suppressing a T cell-	mediated immune response.	· Valori																													
the invention (including agonists or antagonists of the invention)	to modulate IL-10 production	and/or T-cell proliferation	include, for example, assays	such as disclosed and/or cited	in: Robinson, DS, et al., "Th-2	cytokines in allergic disease" Br	Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the contents	of each of which are herein	incorporated by reference in	their entirety. Exemplary cells	that may be used according to	these assays include Th2 cells.	IL10 secreted from Th2 cells	may be measured as a marker of	Th2 cell activation. Th2 cells	are a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation of	Th2 cells play a major role in	the initiation and pathogenesis	of allergy and asthma. Primary	Thelper 2 cells are generated	via in vitro culture under Th2	polarizing conditions using	peripheral blood lymphocytes
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				isolated from cord blood.	
	HBGNC72	446	Production of IL-8	Assays measuring production of	Highly preferred indications
32			by by endothelial	IL-8 are well known in the art	include immunological and
			cells (such as	and may be used or routinely	inflammatory disorders (e.g.,
			Human Umbilical	modified to assess the ability of	such as allergy, asthma,
			Cord Endothelial	polypeptides of the invention	leukemia, etc. and as described
			Cells).	(including antibodies and	below under "Immune Activity",
				agonists or antagonists of the	and "Blood-Related Disorders").
				invention) to regulate	Highly preferred indications
				production and/or secretion of	also includie autoimmune
				IL-8. For example, FMAT may	disorders (e.g., rheumatoid
				be used or routinely modified to	arthritis, systemic lupus
				assess the ability of	erythematosis, Crohn's disease,
				polypeptides of the invention	multiple sclerosis and/or as
				(including antibodies and	described below), neoplastic
_				agonists or antagonists of the	disorders (e.g., organ cancers
				invention) to regulate	such as lung, liver, colon cancer,
				production and/or secretion of	and/or as described below under
*****				IL-8 from endothelial cells	"Hyperproliferative Disorders"),
				(such as human umbilical vein	and cardiovascular disorders
				endothelial cells (HUVEC)).	(e.g. such as described below
				HUVECs are endothelial cells	under "Cardiovascular
				which line venous blood vessels,	Disorders"). Preferred
				and are involved in functions	indications include thrombosis,
				that include, but are not limited	bacteremia and sepsis syndrome
				to, angiogenesis, vascular	and consequent complications
				permeability, vascular tone, and	(such as acute respiratory
				immune cell extravasation.	distress syndrome and systemic
-				Endothelial cells play a pivotal	ischemia-reperfusion resulting
				role in the initiation and	from septic shock), restnosis and
				perpetuation of inflammation	atherosclerosis.
				and secretion of IL-8 may play	

			and activation of immune cells such as neutrophils, macrophages, and lymphocytes.	
HBGNC72	446	Activation of transcription through serum response element in immune cells (such as Tells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional immune response. Additional
15.7	2		446	transcription of transcription through serum response element in immune cells (such as T-cells).

	85:6342-6346 (1988): Benson et	include inflammation and
	al., J Immunol 153(9):3862-	inflammatory disorders, and
	3873 (1994); and Black et al.,	treating joint damage in patients
	Virus Genes 12(2):105-117	with rheumatoid arthritis. An
	(1997), the content of each of	additional highly preferred
	which are herein incorporated	indication is sepsis. Highly
	by reference in its entirety.	preferred indications include
•	Human T cells that may be used	neoplastic diseases (e.g.,
	according to these assays are	leukemia, lymphoma, and/or as
	publicly available (e.g., through	described below under
	the ATCC). Exemplary human	"Hyperproliferative Disorders").
	T cells that may be used	Additionally, highly preferred
	according to these assays	indications include neoplasms
	include the JURKAT cell line,	and cancers, such as, leukemia,
	which is a suspension culture of	lymphoma, melanoma, glioma
	leukemia cells that produce IL-2	(e.g., malignant glioma), solid
	when stimulated.	tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
-		conditions, such as, for example,
		•
		dysplasia. Preferred
		indications include anemia,
		pancytopenia, leukopenia,
		thrombocytopenia, Hodgkin's
		disease, acute lymphocytic
		anemia (ALL), plasmacytomas,
		multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,

granulomators disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	1 Glucose Production in H4IIE	Insulin Secretion of insulin are well-known in the diabetes mellitus. An additional art and may be used or routinely modified to assess the ability of complication associated with polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT disorders as described in the using anti-rat insulin antibodies. A highly preferred indication is a diabeter of indication is a complication associated with diabetic methopathy, kidney disease invention) to stimulate insulin and/or other diseases and secretion is measured by FMAT disorders as described in the lesson and disorders as described in the below), diabetic neuropathy, but and indication is a complication in the complication in the complication is a complication in the complex properties.
	447	447
	HBHAA81	HBHAA81
	33	33

	disregulation is a key	blockage, heart disease, stroke,
	component in diabetes.	impotence (e.g., due to diabetic
	Exemplary assays that may be	neuropathy or blood vessel
	used or routinely modified to	blockage), seizures, mental
	test for stimulation of insulin	confusion, drowsiness,
-	secretion (from pancreatic cells)	nonketotic hyperglycemic-
	by polypeptides of the invention	hyperosmolar coma,
	(including antibodies and	cardiovascular disease (e.g.,
	agonists or antagonists of the	heart disease, atherosclerosis,
	invention) include assays	microvascular disease,
-	disclosed in: Shimizu, H., et al.,	hypertension, stroke, and other
	Endocr J, 47(3):261-9 (2000);	diseases and disorders as
	Salapatek, A.M., et al., Mol	described in the "Cardiovascular
	Endocrinol, 13(8):1305-17	Disorders" section below),
	(1999); Filipsson, K., et al., Ann	dyslipidemia, endocrine
	N Y Acad Sci, 865:441-4	disorders (as described in the
	(1998); Olson, L.K., et al., J	"Endocrine Disorders" section
	Biol Chem, 271(28):16544-52	below), neuropathy, vision
	(1996); and, Miraglia S et. al.,	impairment (e.g., diabetic
-	Journal of Biomolecular	retinopathy and blindness),
	Screening, 4:193-204 (1999),	ulcers and impaired wound
	the contents of each of which is	healing, and infection (e.g.,
	herein incorporated by reference	infectious diseases and disorders
	in its entirety. Pancreatic cells	as described in the "Infectious
	that may be used according to	Diseases" section below,
	these assays are publicly	especially of the urinary tract
	available (e.g., through the	and skin), carpal tunnel
	ATCC) and/or may be routinely	syndrome and Dupuytren's
	generated. Exemplary	contracture). An additional
	pancreatic cells that may be	highly preferred indication is
	used according to these assays	obesity and/or complications
	include HITT15 Cells. HITT15	associated with obesity.
	are an adherent epithelial cell	Additional highly preferred

indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with
line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of
	Production of IFNgamma using a T cells
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	HBHAA81
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	ase		nder	>	•		.၁	e		e.g.,	lg a		L	nse.			tory	red	.၁	<u> </u>	6)		_	_ pec	ative	- p;	ns		ma,	east,	_		her
	tosus dise	oporosis,	l below u	"Infectious Disease"). Highly	preferred indications include	se (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency (e.g.,	/), boostii	ımnne	response, and suppressing a T	cell-mediated immune response.	preferred	•	inflammation and inflammatory	disorders. Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	s (e.g.,	ma,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	as, for	example, leukemia, lymphoma,	melanoma, and prostate, breast,	eatic,	esophageal, stomach, brain,	ancer. Of
	ranuloma	gnant oste	described	ıs Diseas	indicatio	ane disea	id arthriti	thematosi	and/or as	nmunode	sed below	T cell-mediated immune	and supp	ated imm	Additional highly preferred	indications include	ition and	. Additio	ns include	ry fibrosis	indicatio	neoplastic diseases (e.g.,	leukemia, lymphoma,	a, and/or	der "Hyp	s"). Highl	ns include	and cancers, such as, for	leukemia	ia, and pr	lung, colon, pancreatic,	al, stoma	liver and urinary cancer. Other
į	chronic granulomatosus disease	and malignant osteoporosis,	and/or as described below under	"Infection	preferred	autoimmune disease (e.g.,	rheumato	lupus ery	sclerosis	below), in	as described below), boosting a	T cell-me	response,	cell-medi	Additiona	indication	inflamma	disorders	indication	pulmona	preferred	neoplasti	leukemia	melanom	below un	Disorder	indication	and canc	example,	melanom	lung, col	esophage	liver and
	ion	_	the		late					says	latory	luction	rferon		- H			ity of	tion		the	ays	l., J	1:193-	II.,	=	-160	Clin	1995);	ad Sci	n et al.,	49-795	5
	the invent	odies and	gonists of	diate	ion, regu	tivities,	elper cell	mediate	mediated	nplary as:	npomoun	e the proc	ch as Inte	and the	ells. Suc	be used c	ed to test	tory activ	the inven	odies and	gonists of	de the ass	aglia et a	creening 4	vland et a	a practica	ter 6:138	z et al., J	25-233 (ın NY Ac	8); Boehn	unol 15:7	umatolog
	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for immunomodulatory	proteins evaluate the production	of cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad Sci	856:22-32 (1998); Boehm et al.,	Annu Rev Immunol 15:749-795	(1997) and Rheumatology
	polype	(includ	agonist	inventi	immun	inflam	modula	functio	humora	immun	that tes	protein	of cyto	gamma	activat	assays	routine	immun	polype	(includ	agonist	inventi	disclos	Biomo	204 (1	"Lymp	approa	(2000)	Lab Aı	Billian	856:22	Annu]	(1997)
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		_											-						-		**							•					
																						<u></u>	_										

preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example,	hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic	anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,	asthma and allergy. A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus.
(Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human	T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T	lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated	immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
				Activation of transcription through cAMP response element (CRE) in pre-adipocytes.
	·			448
				HBIAC29
				34

HBIAC29 448 Activation of transcription t serum respons element in im cells (such as cells).		J Biol Chem 273:917-923	ulcers and impaired wound
HBIAC29 448		(1998), the contents of each of which are herein incorporated	infectious diseases and disorders
HBIAC29 448		by reference in its entirety. Pre-	as described in the "Infectious
HBIAC29 448		adipocytes that may be used	Diseases" section below,
HBIAC29 448		according to these assays are	especially of the urinary tract
HBIAC29 448	- MAIN-	publicly available (e.g., through	and skin), carpal tunnel
HBIAC29 448		the ATCC) and/or may be	syndrome and Dupuytren's
HBIAC29 448		routinely generated. Exemplary	contracture). Additional highly
HBIAC29 448		mouse adipocyte cells that may	preferred indications are
HBIAC29 448		be used according to these	complications associated with
HBIAC29 448		assays include 3T3-L1 cells.	insulin resistance.
HBIAC29 448	-	3T3-L1 is an adherent mouse	
HBIAC29 448		preadipocyte cell line that is a	
HBIAC29 448		continuous substrain of 3T3	
HBIAC29 448		fibroblast cells developed	
HBIAC29 448		through clonal isolation and	
HBIAC29 448		undergo a pre-adipocyte to	
HBIAC29 448		adipose-like conversion under	
HBIAC29 448		appropriate differentiation	
HBIAC29 448		conditions known in the art.	
		Assays for the activation of	A preferred embodiment of
serum respons element in im cells (such as cells).	transcription through	transcription through the Serum	the invention includes a method
element in im cells (such as cells).	serum response	Response Element (SRE) are	for inhibiting (e.g., reducing)
cells (such as cells).	element in immune	well-known in the art and may	TNF alpha production. An
cells).	cells (such as T-	be used or routinely modified to	alternative preferred
	cells).	assess the ability of	embodiment of the invention
		polypeptides of the invention	includes a method for
		(including antibodies and	stimulating (e.g., increasing)
		agonists or antagonists of the	TNF alpha production.
	-	invention) to regulate the serum	Preferred indications include
		response factors and modulate	blood disorders (e.g., as

		the expression of genes involved	described below under "Immune
		in growth. Exemplary assays	Activity", "Blood-Related
-		for transcription through the	Disorders", and/or
		SRE that may be used or	"Cardiovascular Disorders"),
		routinely modified to test SRE	Highly preferred indications
		activity of the polypeptides of	include autoimmune diseases
		 the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
		antagonists of the invention)	Crohn"s disease, multiple
		 include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
_		 85:6342-6346 (1988); and Black	immune response. Additional
		et al., Virus Genes 12(2):105-	highly preferred indications
		117 (1997), the content of each	include inflammation and
		of which are herein incorporated	inflammatory disorders, and
		 by reference in its entirety. T	treating joint damage in patients
		cells that may be used according	with rheumatoid arthritis. An
		to these assays are publicly	additional highly preferred
		available (e.g., through the	indication is sepsis. Highly
		 ATCC). Exemplary mouse T	preferred indications include
		cells that may be used according	neoplastic diseases (e.g.,
		to these assays include the	leukemia, lymphoma, and/or as
		CTLL cell line, which is an IL-2	described below under
		dependent suspension culture of	"Hyperproliferative Disorders").
		T cells with cytotoxic activity.	Additionally, highly preferred
			indications include neoplasms
·-			and cancers, such as, for
			example, leukemia, lymphoma,
			melanoma, glioma (e.g.,

malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic	anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of	immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,	cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").

	HRIAC29	448	Activation of	Assays for the activation of	Highly preferred indications
27	(2011)) -	transcription through	transcription through the Signal	include allergy, asthma, and
t			STAT6 response	Transducers and Activators of	rhinitis. Additional highly
			element in immune	Transcription (STAT6) response	preferred indications include
			cells (such as mast	element in immune cells (such	infection (e.g., an infectious
,			cells).	as in the human HMC-1 mast	disease as described below
			`	cell line) are well-known in the	under "Infectious Disease"), and
				art and may be used or routinely	inflammation and inflammatory
				modified to assess the ability of	disorders. Preferred indications
				polypeptides of the invention	also include hematopoietic and
				(including antibodies and	immunological disorders (e.g.,
_				agonists or antagonists of the	as described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
		-		modulate the expression of	"Cardiovascular Disorders"),
-				multiple genes. Exemplary	autoimmune diseases (e.g.,
				assays for transcription through	rheumatoid arthritis, systemic
				the STAT6 response element	lupus erythematosis, multiple
				that may be used or routinely	sclerosis and/or as described
				modified to test STAT6	below), and immunodeficiencies
			-	response element activity of the	(e.g., as described below).
				polypeptides of the invention	Preferred indications include
				(including antibodies and	neoplastic diseases (e.g.,
				agonists or antagonists of the	leukemia, lymphoma,
				invention) include assays	melanoma, and/or as described
				disclosed in Berger et al., Gene	below under "Hyperproliferative
				66:1-10 (1998); Cullen and	Disorders"). Preferred
				Malm, Methods in Enzymol	indications include neoplasms
				216:362-368 (1992); Henthorn	and cancer, such as, for
				et al., Proc Natl Acad Sci USA	example, leukemia, lymphoma,
				85:6342-6346 (1988); Sherman,	melanoma, and prostate, breast,
				Immunol Rev 179:48-56 (2001);	lung, colon, pancreatic,
<u>-</u> -				Malaviya and Uckun, J	esophageal, stomach, brain,

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liver and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example,	hyperplasia, metaplasia, alidioi dysplasia. Preferred indications	include hematopoietic and immunological disorders such as	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.			A highly preferred	embodiment of the invention	includes a method for	stimulating the production of	IFNg. An alternative highly			inhibiting th	IFNg. Highly preferred	indications include blood	disorders (e.g., as described
Immunol 168:421-426 (2002); Masuda et al., J Biol Chem 275(38):29331-29337 (2000);	and Masuda et al., J Biol Chem 276:26107-26113 (2001), the	contents of each of which are herein incorporated by reference	in its entirety. Mast cells that	assays are publicly available	(e.g., through the ATCC).	Exemplary human mast cells	that may be used accoluming to these assays include the HMC-1	cell line, which is an immature	human mast cell line established	from the peripheral blood of a	patient with mast cell leukemia,	and exhibits many	characteristics of immature mast	cells.	IFNgamma FMAT. IFNg plays	a central role in the immune	system and is considered to be a	proinflammatory cytokine.	IFNg promotes TH1 and	inhibits TH2 differentiation;	promotes IgG2a and inhibits IgE	secretion; induces macrophage	activation; and increases MHC	expression. Assays for	immunomodulatory proteins
															Production of	IFNgamma using a	T cells								
					,										449										
															HBICW51										
						<u></u>		-								35	<u></u>							_	

produced by T cells and NK cell shat regulate a variety of Activity, "Slood-Related inflammatory activities and may be used or routine by modified to assess the ability of including antibodies and immunomodulation, regulate immunomodulation, assessys that test for immunomodulatory activities, made mediate byothypeptides of the invention imclating antibodies and indications include immunomodulatory activity of including antibodies and indications include indications inclu																	_														\neg
	below under "Immune Activity", "Blood-Related	Disorders', and/or "Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus disease	and malignant osteoporosis,	and/or as described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency (e.g.,	as described below), boosting a	T cell-mediated immune	response, and suppressing a 1	cell-mediated immune response.	Additional highly preferred	indications include	inflammation and inflammatory	disorders. Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliterative	Disorders"). Highly preferred
	produced by T cells and NK cells that regulate a variety of	inflammatory activities and inhibit TH2 helper cell functions	are well known in the art and	may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for immunomodulatory	proteins evaluate the production	of cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical
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				annroach" Chanter 6:138-160	indications include neoplasms
				(2000); Gonzalez et al., J Clin	and cancers, such as, for
				Lab Anal 8(5):225-233 (1995);	example, leukemia, lymphoma,
				Billiau et al., Ann NY Acad Sci	melanoma, and prostate, breast,
				856:22-32 (1998); Boehm et al.,	lung, colon, pancreatic,
				Annu Rev Immunol 15:749-795	esophageal, stomach, brain,
				(1997), and Rheumatology	liver and urinary cancer. Other
				(Oxford) 38(3):214-20 (1999),	preferred indications include
				the contents of each of which	benign dysproliferative
				are herein incorporated by	disorders and pre-neoplastic
				reference in its entirety. Human	conditions, such as, for example,
				T cells that may be used	hyperplasia, metaplasia, and/or
				according to these assays may	dysplasia. Preferred
				be isolated using techniques	indications include anemia,
-				disclosed herein or otherwise	pancytopenia, leukopenia,
				known in the art. Human T	thrombocytopenia, Hodgkin's
				cells are primary human	disease, acute lymphocytic
				lymphocytes that mature in the	anemia (ALL), plasmacytomas,
				thymus and express a T Cell	multiple myeloma, Burkitt's
				receptor and CD3, CD4, or	lymphoma, arthritis, AIDS,
				CD8. These cells mediate	granulomatous disease,
				humoral or cell-mediated	inflammatory bowel disease,
				immunity and may be	sepsis, neutropenia,
				preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted organs
					and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HBJAB02	450	Calcium flux in	Assays for measuring calcium	Preferred embodiments of the

	chondrocytes	flux are well-known in the art	invention include using
		and may be used or routinely	polypeptides of the invention (or
		nolvnentides of the invention	antioodies, agomets, or antaoonists thereoff in defection
		(including antibodies and	diagnosis, prevention, and/or
		agonists or antagonists of the	treatment of Bone and Cartilage
		invention) to mobilize calcium.	Diseases, including but not
		Cells normally have very low	limited to Arthritis, Cartilige
		concentrations of cytosolic	repair, Bone Repair,
		calcium compared to much	Osteoporosis, and related
		higher extracellular calcium.	tumors including
		Extracellular factors can cause	chondrosarcomas,
		an influx of calcium, leading to	chondroblastomas, and
		activation of calcium responsive	chondromas.
		signaling pathways and	
		alterations in cell functions.	
		Exemplary assays that may be	
		used or routinely modified to	
		measure calcium flux in	
		chondrocytes include assays	
		disclosed in: Asada S, et al.,	
		Inflamm Res, 50(1):19-23	
		(2001); Schwartz Z, et al., J	
		Bone Miner Res, 6(7):709-718	
		(1991); Iannotti JP, et al., J	
		Bone Joint Surg Am, 67(1):	
-		113-120 (1985); Sullivan E., et	
-		al., Methods Mol Biol 1999;	
		114:125-133 (1999), the	
		contents of each of which is	
		herein incorporated by reference	
		in its entirety. Cells that may be	
		used according to these assays	

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,	Highly preferred indications include asthma, allergy, hypersensitivity reactions,	inflammation, and inflammatory disorders. Additional highly	preferred indications include immune and hematopoietic	disorders (e.g., as described below under "Immune Activity",	and "Blood-Related Disorders"),	autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting of initiotiting immune cell proliferation.	Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Highly preferred indications
are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include bovine chondrocytes.	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation,	activation, or apoptosis are well known in the art and may be	used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and	agonists or antagonists of the	invention) to promote or inhibit	apoptosis. Exemplary assays for	JNK kinase activity that may be	test JNK kinase-induced activity	of polypeptides of the invention	(including antibodies and	agonists or antagonists of the invention) include the assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Gupta et al., Exp Cell	Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang
	Activation of JNK Signaling Pathway in immune cells	(such as eosinophils).																
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	HBJAB02									M 7								
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include boosting an eosinophil- mediated immune response, and	suppressing an eosinophil-	mediated immune response.																													
and Karin, Nature	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in the	late stage of allergic reactions;	they are recruited to tissues and	mediate the inflammatory	response of late stage allergic	reaction. Moreover, exemplary	assays that may be used or	routinely modified to assess the	ability of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils include	assays disclosed and/or cited in:	Zhang JP, et al., "Role of	caspases in dexamethasone-	induced apoptosis and activation	of c-Jun NH2-terminal kinase	and p38 mitogen-activated	protein kinase in human	eosinophils" Clin Exp Immunol;
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	Immune Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing,
Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils." J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation." J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired
	Glucose Production in H4IIE CD152 in Human T cells
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	HBJAB02
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treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells).							
immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively	on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified	to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or	mediate humoral or cell- mediated immunity. Exemplary assays that test for immunomodulatory proteins	evaluate the upregulation of cell surface markers, such as CD152, and the activation of T cells. Such assays that may be used or routinely modified to	test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for	example, the assays disclosed in Miraglia et al., J

	A highly preferred indication is obesity and/or complications associated with obesity.
Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediated immunity and may be preactivated to enhance responsiveness to	Activation of Assays for the activation of transcription through transcription through the cAMP response element are well-
	Activation of transcription through cAMP response
	451
	HBJAC65
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Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred	indication is diabetes mellitus. An additional highly preferred indication is a complication	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure, nephropathy and/or other diseases and	disorders as described in the "Renal Disorders" section	below), diabetic neuropathy, nerve disease and nerve damage	(e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke,	neuropathy or blood vessel	blockage), seizures, mental confusion, drowsiness,	nonketotic hyperglycemic-	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below), dyslipidemia, endocrine
known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) to increase cAMP.	regulate CREB transcription factors, and modulate expression of genes involved in	a wide variety of cell functions. For example, a 3T3-L1/CRE	reporter assay may be used to identify factors that activate the	cAMP signaling pathway. CREB plays a major role in	adipogenesis, and is involved in differentiation into adipocytes.	CRE contains the binding	sequence for the transcription factor CREB (CRE binding	protein). Exemplary assays for transcription through the cAMP	response element that may be	test cAMP-response element	activity of polypeptides of the	invention (including antibodies and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol
element (CRE) in pre-adipocytes.																

				216:362-368 (1992); Henthorn	disorders (as described in the
				et al., Proc Natl Acad Sci USA	"Endocrine Disorders" section
				85:6342-6346 (1988); Reusch et	below), neuropathy, vision
				al., Mol Cell Biol 20(3):1008-	impairment (e.g., diabetic
				1020 (2000); and Klemm et al.,	retinopathy and blindness),
				J Biol Chem 273:917-923	ulcers and impaired wound
				(1998), the contents of each of	healing, and infection (e.g.,
				which are herein incorporated	infectious diseases and disorders
				by reference in its entirety. Pre-	as described in the "Infectious
				adipocytes that may be used	Diseases" section below,
				according to these assays are	especially of the urinary tract
				publicly available (e.g., through	and skin), carpal tunnel
				the ATCC) and/or may be	syndrome and Dupuytren's
				routinely generated. Exemplary	contracture). Additional highly
				mouse adipocyte cells that may	preferred indications are
				be used according to these	complications associated with
				assays include 3T3-L1 cells.	insulin resistance.
				3T3-L1 is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
37	HBJAC65	451	SEAP in OE-33		
	HBJAC65	451	Activation of	Assays for the activation of	Highly preferred indications
37			transcription through	transcription through the	include neoplastic diseases (e.g.,
			GAS response	Gamma Interferon Activation	leukemia, lymphoma, and/or as
			element in immune	Site (GAS) response element are	described below under

described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus disease	and malignant osteoporosis,	and/or an infectious disease as	described below under	"Infectious Disease"). An	additional preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas, multiple	myeloma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease, and	asthma and allergy.	A highly preferred embodiment
1. Toolle and as the	SUJPT cell line, that may be used	according to these assays are	publicly available (e.g., through	the ATCC).													-1														IL-6 FMAT. IL-6 is produced
																															Production of IL-6
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of the invention includes a method for stimulating (e.g.,	increasing) IL-6 production. An	alternative highly preferred	embodiment of the invention	includes a method for inhibiting	(e.g., reducing) IL-6 production.	A highly preferrred indication is	the stimulation or enhancement	of mucosal immunity. Highly	preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as described	below under "Infectious	Disease"). Highly preferred	indications include autoimmune	diseases (e.g., rheumatoid	arthritis, systemic lupus	erythematosis, multiple sclerosis	and/or as described below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response and	alternatively suppressing a B	cell-mediated immune response.	Highly preferred indications	include inflammation and
by T cells and has strong effects on B cells. IL-6 participates in	IL-4 induced IgE production	and increases IgA production	(IgA plays a role in mucosal	immunity). IL-6 induces	cytotoxic T cells. Deregulated	expression of IL-6 has been	linked to autoimmune disease,	plasmacytomas, myelomas, and	chronic hyperproliferative	diseases. Assays for	immunomodulatory and	differentiation factor proteins	produced by a large variety of	cells where the expression level	is strongly regulated by	cytokines, growth factors, and	hormones are well known in the	art and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and the	stimulation and upregulation of
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38								·																		-					

inflammatory disorders.Additional highly preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma,	leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease,	Inflammatory bowel disease, sepsis, neutropenia,
T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J	Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation	and functional activities.
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neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious		A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel
		Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells.
	SEAP in UMR-106	Regulation of viability and proliferation of pancreatic beta cells.
	453	454
,	HBJDS79	HBJEL16
	39	40

blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract	and skin), carpal tunnel	syndrome and Dupuytren's	contracture). An additional	highly preferred indication is	obesity and/or complications	associated with obesity.	Additional highly preferred	indications include weight loss		Additional highly preferred
Exemplary assays that may be used or routinely modified to test regulation of viability and	proliferation of pancreatic beta	cells by polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) include assays	al Mol Endocrinol, 15(1):136-	48 (2001); Huotari MA, et al.,	Endocrinology, 139(4):1494-9	(1998); Hugl SR, et al., J Biol	Chem 1998 Jul	10;273(28):17771-9 (1998), the	contents of each of which is	herein incorporated by reference	in its entirety. Pancreatic cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be routinely	generated. Exemplary	pancreatic cells that may be	used according to these assays	include rat INS-1 cells. INS-1	cells are a semi-adherent cell	line established from cells	isolated from an X-ray induced	rat transplantable insulinoma.	These cells retain characteristics	typical of native pancreatic beta	cells including glucose inducible
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				-								-						_										

			· ·	insulin secretion. References:	indications are complications
				Asfari et al. Endocrinology	associated with insulin
				1992 130:167.	resistance.
	HBJEL16	454	Production of	Assays for measuring	Highly preferred indications
40			VCAM in	expression of VCAM are well-	include inflammation (acute and
			endothelial cells	known in the art and may be	chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and inflammatory
				agonists or antagonists of the	disorders, immunological
				invention) to regulate VCAM	disorders, neoplastic disorders
			•	expression. For example,	(e.g. cancer/tumorigenesis), and
				FMAT may be used to meaure	cardiovascular disorders (such
				the upregulation of cell surface	as described below under
				VCAM-1 expresssion in	"Immune Activity", "Blood-
				endothelial cells. Endothelial	Related Disorders",
				cells are cells that line blood	"Hyperproliferative Disorders"
				vessels, and are involved in	and/or "Cardiovascular
				functions that include, but are	Disorders"). Highly preferred
				not limited to, angiogenesis,	indications include neoplasms
				vascular permeability, vascular	and cancers such as, for
				tone, and immune cell	example, leukemia, lymphoma,
				extravasation. Exemplary	melanoma, renal cell carcinoma,
				endothelial cells that may be	and prostate, breast, lung, colon,
				used according to these assays	pancreatic, esophageal, stomach,
				include human umbilical vein	brain, liver and urinary cancer.
				endothelial cells (HUVEC),	Other preferred indications
				which are available from	include benign dysproliferative
				commercial sources. The	disorders and pre-neoplastic
				expression of VCAM (CD106),	conditions, such as, for example,
				a membrane-associated protein,	hyperplasia, metaplasia, and/or

dysplasia.	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic
can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved in differentiation into adipocytes. CRE contains the binding sequence for the transcription
	Activation of transcription through cAMP response element (CRE) in pre-adipocytes.
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	HBJFK45
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neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section	below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.
factor CREB (CRE binding protein). Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to	test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch et al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the contents of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3
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				fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation	
41	HBJFK45	455	Activation of transcription through NFAT response element in immune cells (such as natural	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
			killer cells).	may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT	"Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as
				transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to	described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred
				test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include

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neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under	"Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as,	for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative	conditions, such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's	disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,
216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al. Int J Biochem Cell Biol	31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and	Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by	reference in its entirety. NK cells that may be used according to these assays are publicly	available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-	YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	
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					meningitis, Lyme Disease, asthma and allergy.
,	HBJFK45	455	Activation of	Assays for the activation of	Highly preferred indications
41			transcription through	transcription through the Gamma Interferon Activation	nciude neopiastic diseases (e.g., leukemia, lymphoma, and/or as
			element in immune	Site (GAS) response element are	described below under
			cells (such as T-	well-known in the art and may	"Hyperproliferative Disorders").
			cells).	be used or routinely modified to	Highly preferred indications
			`	assess the ability of	include neoplasms and cancers,
				polypeptides of the invention	such as, for example, leukemia,
				(including antibodies and	lymphoma (e.g., T cell
				agonists or antagonists of the	lymphoma, Burkit's
				invention) to regulate STAT	lymphoma, non-Hodgkins
				transcription factors and	lymphoma, Hodgkin"s disease),
				modulate gene expression	melanoma, and prostate, breast,
				involved in a wide variety of	lung, colon, pancreatic,
				cell functions. Exemplary	esophageal, stomach, brain,
				assays for transcription through	liver and urinary cancer. Other
				the GAS response element that	preferred indications include
				may be used or routinely	benign dysproliferative
				modified to test GAS-response	disorders and pre-neoplastic
				element activity of polypeptides	conditions, such as, for example,
				of the invention (including	hyperplasia, metaplasia, and/or
				antibodies and agonists or	dysplasia. Preferred indications
				antagonists of the invention)	include autoimmune diseases
				include assays disclosed in	(e.g., rheumatoid arthritis,
				Berger et al., Gene 66:1-10	systemic lupus erythematosis,
				(1998); Cullen and Malm,	multiple sclerosis and/or as
				Methods in Enzymol 216:362-	described below),
_				368 (1992); Henthorn et al.,	immunodeficiencies (e.g., as
				Proc Natl Acad Sci USA	described below), boosting a T
				85:6342-6346 (1988);	cell-mediated immune response,

Matikainen et al., Blood mediated immune response. 93(6):1980-1991 (1999); and Hentinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary herein incorporated by reference blood disorders (e.g., as human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through referror of the that may be used according to these assays are publicly available (e.g., through and infection (e.g., viral infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AlDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune				•		<u> </u>												S	-		_		_	_o						
	nd suppressing a T cell- ediated immune response.	dditional preferred indications clude inflammation and	flammatory disorders. Highly	referred indications include	lood disorders (e.g., as	escribed below under "Immune	ctivity", "Blood-Related	isorders", and/or	Cardiovascular Disorders"),	nd infection (e.g., viral	fections, tuberculosis,	fections associated with	hronic granulomatosus disease	nd malignant osteoporosis,	nd/or an infectious disease as	escribed below under	Infectious Disease"). An	dditional preferred indication is	liopathic pulmonary fibrosis.	referred indications include	nemia, pancytopenia,	ukopenia, thrombocytopenia,	cute lymphocytic anemia	ALL), plasmacytomas, multiple	1yeloma, arthritis, AIDS,	ranulomatous disease,	iflammatory bowel disease,	epsis, neutropenia,	eutrophilia, psoriasis,	uppression of immune
				e			pasn a				ü	u	d	an	an	ap	,	<u>ac</u>	pi.	Pı	ar	e	ac	4)	<u> </u>	<u>p</u>	ui	Se)U	18

					and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
42	HBJKD16	456	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as

differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.	differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.	preferred indications also	include boosting a B cell-	mediated immune response and	alternatively suppressing a B	cell-mediated immune response.	Highly preferred indications	include inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include anemia, pancytopenia,	•
		differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and the	stimulation and upregulation of	T cell proliferation and	functional activities. Such	assays that may be used or	routinely modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	

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Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infectiou (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate
	Production of MIP1alpha
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Preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,
chemotaxis, and modulate T cell	differentiation. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and Eremin,	J R Coll Surg Ednb 45(1):9-19	(2001); Drakes et al., Transp	Immunol 8(1):17-29 (2000);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its
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meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage
entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to
	Stimulation of Calcium Flux in pancreatic beta cells.
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	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract	and skin), carpal tunnel	d Dub	contracture). An additional	highly preferred indication is	obecity and/or complications
	much higher extracellular	calcium. Extracellular factors	can cause an influx of calcium,	leading to activation of calcium	responsive signaling pathways	and alterations in cell functions.	Exemplary assays that may be	used or routinely modified to	measure calcium flux by	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in: Satin LS, et al.,	Endocrinology, 136(10):4589-	601 (1995); Mogami H, et al.,	Endocrinology, 136(7):2960-6	(1995); Richardson SB, et al.,	Biochem J, 288 (Pt 3):847-51	(1992); and, Meats, JE, et al.,	Cell Calcium 1989 Nov-	Dec;10(8):535-41 (1989), the	contents of each of which is	herein incorporated by reference	in its entirety. Pancreatic cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be routinely	generated. Exemplary	pancreatic cells that may be	used according to these assays	
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associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred
are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
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	HBJKD16
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indications include neoplasms and cancers such as, for	example, leukemia, lymphoma, melanoma, renal cell carcinoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer.	Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example,	hyperplasia, metaplasia, and/or dysplasia.		A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include	blood disorders (e.g., as
not limited to, angiogenesis, vascular permeability, vascular	tone, and immune cell extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein	endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106),	a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of	lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory		response factors and modulate
					Activation of transcription through serum response element in immune cells (such as Teells).	
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					HBMBM96	
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			baylovni sanas on ociosaruva att	described below under "Immune
_			in growth. Exemplary assays	Activity", "Blood-Related
			for transcription through the	Disorders", and/or
			SRE that may be used or	"Cardiovascular Disorders"),
			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
			antagonists of the invention)	Crohn"s disease, multiple
			include assays disclosed in	sclerosis and/or as described
			Berger et al., Gene 66:1-10	below), immunodeficiencies
			(1998); Cullen and Malm,	(e.g., as described below),
			Methods in Enzymol 216:362-	boosting a T cell-mediated
			368 (1992); Henthorn et al.,	immune response, and
			Proc Natl Acad Sci USA	suppressing a T cell-mediated
			85:6342-6346 (1988); and Black	immune response. Additional
			et al., Virus Genes 12(2):105-	highly preferred indications
			117 (1997), the content of each	include inflammation and
	-		of which are herein incorporated	inflammatory disorders, and
			by reference in its entirety. T	treating joint damage in patients
			cells that may be used according	with rheumatoid arthritis. An
			to these assays are publicly	additional highly preferred
			available (e.g., through the	indication is sepsis. Highly
			ATCC). Exemplary mouse T	preferred indications include
			cells that may be used according	neoplastic diseases (e.g.,
			to these assays include the	leukemia, lymphoma, and/or as
			CTLL cell line, which is an IL-2	described below under
			dependent suspension culture of	"Hyperproliferative Disorders").
			T cells with cytotoxic activity.	Additionally, highly preferred
				indications include neoplasms
				and cancers, such as, for
				example, leukemia, lymphoma,
				melanoma, glioma (e.g.,

malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esonhageal stomach, brain.	liver and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Preferred indications include anemia,	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's	disease, acute lymphocytic	multiple myeloma, Burkitt's	lympnoma, artnrius, AIDS, granulomatous disease,	inflammatory bowel disease,	psoriasis, suppression of	immune reactions to	transplanted organs and tissues, hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	infection (e.g., an infectious	disease as described below under "Infectious Disease").
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Immune Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of	preventing, detecting, diagnosting, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells).
CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may	immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the unregulation of
CD152 in Human T	
458	
HBMBX01	
44	

cell surface markers, such as	cells. Such assays that may be	used or routinely modified to	test immunomodulatory	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include, for	example, the assays disclosed	in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); McCoy et al., Immunol	Cell Biol 77(1):1-10 (1999);	Oostervegal et al., Curr Opin	Immunol 11(3):294-300	(1999); and Saito T, Curr Opin	Immunol 10(3):313-321	(1998), the contents of each of	which are herein incorporated	by reference in its entirety.	Human T cells that may be	used according to these assays	may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human T cells are primary	human lymphocytes that
							-																						

				mature in the thymus and	
				Illature in the trigings and	
				express a T Cell receptor and	
				CD3, CD4, or CD8. These	
				cells mediate humoral or cell-	
				mediated immunity and may	
			-	be preactivated to enhance	
				responsiveness to	
				immunomodulatory factors.	
	HRMRX01	458	Production of IL-8	Assays measuring production of	Highly preferred indications
77	INTERIOR)) -	by by endothelial	IL-8 are well known in the art	include immunological and
1			cells (such as	and may be used or routinely	inflammatory disorders (e.g.,
			Human Umbilical	modified to assess the ability of	such as allergy, asthma,
			Cord Endothelial	nolvnentides of the invention	leukemia, etc. and as described
			Cold Ellaction	Girchding antibodies and	below under "Immune Activity",
			cells).	agonists or antagonists of the	and "Blood-Related Disorders").
				invention) to regulate	Highly preferred indications
				production and/or secretion of	also includie autoimmune
				II8 For example, FMAT may	disorders (e.g., rheumatoid
				be used or routinely modified to	arthritis, systemic lupus
				assess the ability of	erythematosis, Crohn"s disease,
				nolypeptides of the invention	multiple sclerosis and/or as
				(including antibodies and	described below), neoplastic
				agonists or antagonists of the	disorders (e.g., organ cancers
				invention) to regulate	such as lung, liver, colon cancer,
				production and/or secretion of	and/or as described below under
				IL-8 from endothelial cells	"Hyperproliferative Disorders"),
				(such as human umbilical vein	and cardiovascular disorders
				endothelial cells (HUVEC)).	(e.g. such as described below
			-	HUVECs are endothelial cells	under "Cardiovascular
			,	which line venous blood vessels,	Disorders"). Preferred
				and are involved in functions	indications include thrombosis,
				that include, but are not limited	bacteremia and sepsis syndrome

and consequent complications a., and (such as acute respiratory distress syndrome and systemic ivotal ischemia-reperfusion resulting from septic shock), restnosis and atherosclerosis. y play iitment cells ocytes.	on in Diabetes A highly preferred indication is diabetes. Additional highly preferred indications include to complications associated with diabetes (e.g., diabetic nephropathy, can be kidney disease (e.g., renal failure, ith nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), ce in its blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart cardiovascular disease (e.g., heart
to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of inflammation and secretion of IL-8 may play an important role in recruitment and activation of immune cells such as neutrophils,	SEAP in OE-21 Activation of transcription in OE-21 Epithelial Human Caucasian oesophageal squamous cell carcinoma. HLA-A,-B and -C (MHC class I) are expressed constitutively, expression of ICAM-1 can be induced by treatment with interferon-gamma. OE21 cells express epithelial cytokeratins and are tumourigenic in nude mice. Br J Cancer 1997;75:258, which is herein incorporated by reference in its entirety.
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disease atherosclerosis.	microvascular disease,	hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine disorders	(as described in the Endocrine Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the urinary	tract and skin). Highly preferred	indications also include obesity,	weight gain, and weight loss, as	well as complications associated	with obesity, weight gain, and	weight loss. Preferred	embodiments of the invention	include methods of preventing,	detecting, diagnosing, treating	and/or ameliorating the above	mentioned conditions, disorders,	and diseases.				oduction increasing) IL-0 production: All
					, , , ,							-					-											by T cells and has strong effects	on B cells. IL-6 participates in	IL-4 induced IgE production
	-												-														Production of IL-6			
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embodiment of the invention includes a method for inhibiting	(e.g., reducing) IL-6 production.	A highly preferrred indication is	the stimulation or enhancement	of mucosal immunity. Highly	preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as described	below under "Infectious	Disease"). Highly preferred	indications include autoimmune	diseases (e.g., rheumatoid	arthritis, systemic lupus	erythematosis, multiple sclerosis	and/or as described below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response and	alternatively suppressing a B	cell-mediated immune response.	Highly preferred indications	include inflammation and	inflammatory	disorders. Additional highly	preferred indications include	asthma and allergy. Highly
(IgA plays a role in mucosal immunity). IL-6 induces	cytotoxic T cells. Deregulated	expression of IL-6 has been	linked to autoimmune disease,	plasmacytomas, myelomas, and	chronic hyperproliferative	diseases. Assays for	immunomodulatory and	differentiation factor proteins	produced by a large variety of	cells where the expression level	is strongly regulated by	cytokines, growth factors, and	hormones are well known in the	art and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and the	stimulation and upregulation of	T cell proliferation and	functional activities. Such	assays that may be used or	routinely modified to test
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		immunomodulatory and	preferred indications include
100		diffferentiation activity of	neoplastic diseases (e.g.,
-	-	polypeptides of the invention	myeloma, plasmacytoma,
-		(including antibodies and	leukemia, lymphoma,
		agonists or antagonists of the	melanoma, and/or as described
		invention) include assays	below under "Hyperproliferative
		disclosed in Miraglia et al., J	Disorders"). Highly preferred
		Biomolecular Screening 4:193-	indications include neoplasms
		204(1999); Rowland et al.,	and cancers, such as, myeloma,
		"Lymphocytes: a practical	plasmacytoma, leukemia,
		approach" Chapter 6:138-160	lymphoma, melanoma, and
		(2000); and Verhasselt et al., J	prostate, breast, lung, colon,
		Immunol 158:2919-2925	pancreatic, esophageal, stomach,
		(1997), the contents of each of	brain, liver and urinary cancer.
		which are herein incorporated	Other preferred indications
		by reference in its entirety.	include benign dysproliferative
		Human dendritic cells that may	disorders and pre-neoplastic
		be used according to these	conditions, such as, for example,
		assays may be isolated using	hyperplasia, metaplasia, and/or
		techniques disclosed herein or	dysplasia. Preferred indications
		otherwise known in the art.	include anemia, pancytopenia,
		Human dendritic cells are	leukopenia, thrombocytopenia,
		antigen presenting cells in	Hodgkin's disease, acute
		suspension culture, which, when	lymphocytic anemia (ALL),
		activated by antigen and/or	multiple myeloma, Burkitt's
		cytokines, initiate and	lymphoma, arthritis, AIDS,
		upregulate T cell proliferation	granulomatous disease,
		and functional activities.	inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,
-			suppression of immune
			reactions to transplanted organs
			and tissues, hemophilia,

					hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious Disease")
	UDMIIU74	760	Activation of INK	Kinase assav. JNK kinase	Highly preferred indications
46	TDIMICII /	00	Signaling Pathway	assays for signal transduction	include asthma, allergy,
2 + 			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are well	inflammation, and inflammatory
			eosinophils).	known in the art and may be	disorders. Additional highly
<u> </u>			•	used or routinely modified to	preferred indications include
				assess the ability of	immune and hematopoietic
				polypeptides of the invention	disorders (e.g., as described
				(including antibodies and	below under "Immune Activity",
				agonists or antagonists of the	and "Blood-Related Disorders"),
		-		invention) to promote or inhibit	autoimmune diseases (e.g.,
				cell proliferation, activation, and	rheumatoid arthritis, systemic
				apoptosis. Exemplary assays for	lupus erythematosis, Crohn"s
				JNK kinase activity that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
				test JNK kinase-induced activity	immunodeficiencies (e.g., as
				of polypeptides of the invention	described below). Highly
				(including antibodies and	preferred indications also
				agonists or antagonists of the	include boosting or inhibiting
				invention) include the assays	immune cell proliferation.
				disclosed in Forrer et al., Biol	Preferred indications include
	_			Chem 379(8-9):1101-1110	neoplastic diseases (e.g.,
				(1998); Gupta et al., Exp Cell	leukemia, lymphoma, and/or as
				Res 247(2): 495-504 (1999);	described below under

"Hyperproliferative Disorders"). Highly preferred indications include boosting an eosinophilmediated immune response, and suppressing an eosinophilmediated immune response.		
Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999);	the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of Calum MH2-terminal kinase	and p38 mitogen-activated

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section
protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis.
	Regulation of transcription of Malic Enzyme in adipocytes
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below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel	blockage), seizures, mental confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract	and skin), carpal tunnel	syndrome and Dupuytren's	contracture). An additional
Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME	promoter contains two direct repeat (DR1)- like elements	MEp and MEd identified as putative PPAR response	elements. ME promoter may also responds to API and other	transcription factors.	Exemplary assays that may be	used of routinely modified to test for regulation of	transcription of Malic Enzyme	(in adipoocytes) by polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in:	Streeper, R.S., et al., Mol	Endocrinol, 12(11):1778-91	(1998); Garcia-Jimenez, C., et	al., Mol Endocrinol, 8(10):1361-	9 (1994); Barroso, I., et al., J	Biol Chem, 274(25):17997-8004	(1999); Ijpenberg, A., et al., J	Biol Chem, 272(32):20108-	20117 (1997); Berger, et al.,	Gene 66:1-10 (1988); and,	Cullen, B., et al., Methods in	Enzymol. 216:362–368 (1992),	the contents of each of which is	herein incorporated by reference
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s that hese le le und/or l. t. may rat	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in and increases IgA production alternative highly preferred indication is linked to autoimmune disease. Assays for cells where the expression level differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and indications include autoimmune modified to assess the ability of diseases (e.g., rheumatoid modified at assess the ability of diseases (e.g., reducing) IL-6 production. An alternative highly preferred embodiment of the invention increasing) IL-6 production. An alternative highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indication is call where the expression level and infection (e.g., as and/or cells where the expression level art and may be used or routinely indications include autoimmune modified to assess the ability of diseases (e.g., reducing). IL-6 production. An alternative highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indication is call where the expression level and infection (e.g., as described below under "Immune disease"), and infections include autoimmune modified to assess the ability of diseases.
	Production of IL-6 FMAT. IL-6 is produce by T cells and has strong e on B cells. IL-6 participate IL-4 induced IgE production and increases IgA production in mucos immunity). IL-6 induces cytotoxic T cells. Deregule expression of IL-6 has bee linked to autoimmune dise plasmacytomas, myelomas chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor prote produced by a large variety cells where the expression is strongly regulated by cytokines, growth factors, hormones are well known art and may be used or roumodified to assess the abili
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arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as	described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cellmediated immune response.	Highly preferred indications include inflammation and inflammatory disorders. Additional highly	preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma,	meianoma, and of as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins	cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such	assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	(2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may

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disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma,	melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic
agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of genes important for Th2 immune response development. Exemplary assays for transcription through the GATA3 response element that	may be used or routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. T cells that may

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conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, Hodgkin's disease),
a, metapa Prefera Prefera include nia, leuk topenia, disease, ic anemi somas, m Burkitt's IDS, gra flammat psis, neu psis, neu ia, psorie n of imn o transpl t, hemop ulation, and Ly	oplastic lymphor below ur ferred ir ferred ir examp r examp (e.g., T (e.g., T hodgk i, Hodgk i, Hodgk i, Hodgk is poplastic in the control of
conditions, such as, for exan hyperplasia, metaplasia, and dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, leukemia Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphor arthritis, AIDS, granulomate disease, inflammatory bowe disease, inflammatory bowe disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organd tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disea	Highly preferred indicatio include neoplastic diseases (leukemia, lymphoma, and/or described below under "Hyperproliferative Disorder Highly preferred indications include neoplasms and cance such as, for example, leuker lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, Hodgkin's disea
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be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is a suspension culture of IL-2 dependent T cells that also respond to IL-4.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and
be used accordin assays are public (e.g., through the Exemplary mous may be used accassays include th which is a susper IL-2 dependent 7 respond to IL-4.	Assays for the activation transcription through the Gamma Interferon Activa Site (GAS) response elem well-known in the art and be used or routinely modi assess the ability of polypeptides of the inven (including antibodies and agonists or antagonists of transcription factors and transcription factors and
be used assays a (e.g., thu Exemple may be assays ii which is IL-2 dep respond	Assays transcri Gamma Site (G, well-kn be used assess th polypep (includi agonists inventici transcri
	f through se nmune s T-
	Activation of transcription through GAS response element in immune cells (such as T-cells).
	Activa transc GAS deleme cells (cells).
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	modulate gene expression	melanoma, and prostate, breast,
	 involved in a wide variety of	lung, colon, pancreatic,
	cell functions. Exemplary	esophageal, stomach, brain,
	assays for transcription through	liver and urinary cancer. Other
	the GAS response element that	preferred indications include
	may be used or routinely	benign dysproliferative
	modified to test GAS-response	disorders and pre-neoplastic
	element activity of polypeptides	conditions, such as, for example,
	of the invention (including	hyperplasia, metaplasia, and/or
	antibodies and agonists or	dysplasia. Preferred
	antagonists of the invention)	indications include autoimmune
	include assays disclosed in	diseases (e.g., rheumatoid
	Berger et al., Gene 66:1-10	arthritis, systemic lupus
	(1998); Cullen and Malm,	erythematosis, multiple sclerosis
	Methods in Enzymol 216:362-	and/or as described below),
	368 (1992); Henthorn et al.,	immunodeficiencies (e.g., as
	Proc Natl Acad Sci USA	described below), boosting a T
	85:6342-6346 (1988);	cell-mediated immune response,
	Matikainen et al., Blood	and suppressing a T cell-
	 93(6):1980-1991 (1999); and	mediated immune response.
	Henttinen et al., J Immunol	Additional preferred indications
	155(10):4582-4587 (1995), the	include inflammation and
	contents of each of which are	inflammatory disorders.
	herein incorporated by reference	Highly preferred indications
	in its entirety. Exemplary	include blood disorders (e.g., as
	mouse T cells that may be used	described below under "Immune
	according to these assays are	Activity", "Blood-Related
	publicly available (e.g., through	Disorders", and/or
	the ATCC). Exemplary T cells	"Cardiovascular Disorders"),
	that may be used according to	and infection (e.g., viral
-	these assays include the CTLL	infections, tuberculosis,
	cell line, which is a suspension	infections associated with
	culture of IL-2 dependent	chronic granulomatosus disease

and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preterred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly
cytotoxic T cells.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Activation of Natural Killer Cell ERK Signaling Pathway.
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preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative	highly preferred embodiment of the invention includes a method for inhibiting natural killer cell	differentiation. Highly preferred indications include neoplastic diseases (e.g., as	"Hyperproliferative Disorders"), blood disorders (e.g., as	Activity", "Cardiovascular Disorders", and/or "Blood-	Related Disorders"), immune disorders (e.g., as described	below under "Immune Activity") and infections (e.g., as described below under	"Infectious Disease"). Preferred indications include	blood disorders (e.g., as described below under "Immune Activity" "Rlood-Related	Disorders", and/or "Cardiovascular Disorders").	Highly preferred indications include autoimmune diseases	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
(including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and	differentiation. Exemplary assays for ERK kinase activity that may be used or routinely	modified to test ERK kinase- induced activity of polypeptides of the invention (including	antagonists of the invention) include the assays disclosed in Forrer et al. Biol Chem 379(8.	9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-	48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001);	and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of	which are herein incorporated by reference in its entirety.	Natural killer cells that may be used according to these assays	through the ATCC). Exemplary natural killer cells that may be	used according to these assays include the human natural killer	cell lines (for example, NK-YT cells which have cytolytic and
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described below) and imminodeficiencies (e.g., as	described below). Additional	highly preferred indications	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary cancer, lymphoma	and leukemias. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Other highly preferred	indications include,	pancytopenia, leukopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), arthritis, asthma, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, psoriasis, immune	reactions to transplanted organs	and tissues, endocarditis,	meningitis, Lyme Disease, and	allergies.	A preferred embodiment of
NK cells.																													Assays for the activation of
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preferred indications include	neopiastic diseases (e.g., leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophilia,	psoriasis, suppression of	immune reactions to
ATCC). Exemplary mouse T	cells that may be used according to these assays include the	CTLL cell line, which is an IL-2	dependent suspension culture of	T cells with cytotoxic activity.																											
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transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders. An additional highly preferred inflammation is infection
	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies
	Activation of transcription through NFAT response in immune cells (such as T-cells).
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(e.g., an infectious disease as described below under	Infectious Disease). Preferred indications include	neoplastic diseases (e.g.,	described below under	"Hyperproliferative Disorders").	Preferred indications include	neoplasms and cancers, such as,	for example, leukemia,	lymphoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications also include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune
the invention) include assays disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer et	al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. T cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC). Exemplary human T	cells that may be used according	to these assays include the	JURKAT cell line, which is a	suspension culture of leukemia	cells that produce IL-2 when	stimulated.					
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reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred indication is transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of assess and agonists or antagonists of the invention) to activate the DMEF1 response element in reporter construct (such as that containing the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin responsive glucose transporter in fat and
	Regulation of transcription via DMEF1 response element in adipocytes and preadipocytes
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diseases and disorders as described in the "Cardiovascular Disorders" section below),	dysuptaemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision	impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound	nealing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below,	especially of the urinary tract and skin). An additional highly preferred indication is obesity	and/or complications associated with obesity. Additional highly preferred indications include	weight loss or alternatively, weight gain. Additional highly preferred indications are	complications associated with insulin resistance.		
modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes)	by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol	Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair	regulatory element and novel DNA binding protein that	promoter in transgenic mice", J Biol Chem. 2000 Aug	al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992),	the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used	according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary	cells that may be used according to these assays include the
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HBX	mouse 3T3-L1 cell line which is an adherent mouse preadipocyte	are a continuous substrain of	through clonal isolation. These	cells undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	CX15 467 Activation of Assays for the activation of A highly preferred indication is	transcription through transcription through the cAMP	element (CRE) in known in the art and may be Additional highly preferred	pre-adipocytes. used or routinely modified to indications include weight loss	polypeptides of the invention An additional highly preferred	 agonists or antagonists of the An additional highly preferred	•	regulate CREB transcription associated with diabetes (e.g.,	factors, and modulate diabetic retinopathy, diabetic		For example, a 3T3-L1/CRE and/or other diseases and	_	identify factors that activate the "Renal Disorders" section	cAMP signaling pathway. below), diabetic neuropathy,	CREB plays a major role in nerve disease and nerve damage	adipogenesis, and is involved in (e.g., due to diabetic	
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impotence (e.g., due to diabetic neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract	and skin), carpal tunnel	syndrome and Dupuytren's	contracture). Additional highly	preferred indications are	complications associated with	insulin resistance.		
sequence for the transcription factor CREB (CRE binding	protein). Exemplary assays for	transcription through the cAMP	response element that may be	used or routinely modified to	test cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch et	al., Mol Cell Biol 20(3):1008-	1020 (2000); and Klemm et al.,	J Biol Chem 273:917-923	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g., through	the ATCC) and/or may be	routinely generated. Exemplary	mouse adipocyte cells that may	be used according to these	assays include 3T3-L1 cells.	3T3-L1 is an adherent mouse	preadipocyte cell line that is a
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				fihroplast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
	-			appropriate differentiation	
				conditions known in the art.	
	5	467	Activation of	Assays for the activation of	A highly preferred indication is
		2	transcription through	transcription through the Serum	obesity and/or complications
			seriim response	Response Element (SRE) are	associated with obesity.
	_		element in pre-	well-known in the art and may	Additional highly preferred
			adipocytes.	be used or routinely modified to	indications include weight loss
			•	assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to regulate the serum	indication is a complication
				response factors and modulate	associated with diabetes (e.g.,
				the expression of genes involved	diabetic retinopathy, diabetic
				in growth. Exemplary assays	nephropathy, kidney disease
				for transcription through the	(e.g., renal failure, nephropathy
				SRE that may be used or	and/or other diseases and
	•			routinely modified to test SRE	disorders as described in the
				activity of the polypeptides of	"Renal Disorders" section
		٠		the invention (including	below), diabetic neuropathy,
				antibodies and agonists or	nerve disease and nerve damage
				antagonists of the invention)	(e.g., due to diabetic
				include assays disclosed in	neuropathy), blood vessel
				Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
				(1998); Cullen and Malm,	impotence (e.g., due to diabetic
				Methods in Enzymol 216:362-	neuropathy or blood vessel
				368 (1992); Henthorn et al.,	blockage), seizures, mental

confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below). Additional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and
Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
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			for the activation of	inflammation and inflammatory
			transcription through the	disorders. Preferred indications
	-		GATA3 response element are	also include blood disorders
			well-known in the art and may	(e.g., as described below under
			be used or routinely modified to	"Immune Activity", "Blood-
			assess the ability of	Related Disorders", and/or
			polypeptides of the invention	"Cardiovascular Disorders").
			(including antibodies and	Preferred indications include
			agonists or antagonists of the	autoimmune diseases (e.g.,
			invention) to regulate GATA3	rheumatoid arthritis, systemic
			transcription factors and	lupus erythematosis, multiple
		-	modulate expression of mast	sclerosis and/or as described
			cell genes important for immune	below) and immunodeficiencies
			response development.	(e.g., as described below).
			Exemplary assays for	Preferred indications include
			transcription through the	neoplastic diseases (e.g.,
			GATA3 response element that	leukemia, lymphoma,
			may be used or routinely	melanoma, prostate, breast,
			modified to test GATA3-	lung, colon, pancreatic,
			response element activity of	esophageal, stomach, brain,
			polypeptides of the invention	liver, and urinary tract cancers
			(including antibodies and	and/or as described below under
			agonists or antagonists of the	"Hyperproliferative Disorders").
			invention) include assays	Other preferred indications
			disclosed in Berger et al., Gene	include benign dysproliferative
			66:1-10 (1998); Cullen and	disorders and pre-neoplastic
-			Malm, Methods in Enzymol	conditions, such as, for example,
			216:362-368 (1992); Henthorn	hyperplasia, metaplasia, and/or
	****		et al., Proc Natl Acad Sci USA	dysplasia. Preferred indications
			85:6342-6346 (1988); Flavell et	include anemia, pancytopenia,
			al., Cold Spring Harb Symp	leukopenia, thrombocytopenia,
			Quant Biol 64:563-571 (1999);	leukemias, Hodgkin's disease,
			Rodriguez-Palmero et al., Eur J	acute lymphocytic anemia

(ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, mellitus, and Lyme Disease.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under
Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
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"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple		leukemia, lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver, and urinary tract cancers and/or as described below under "Hyperproliferative Disorders"). Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias Hodokin's disease.	acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel
are well-known in the art and may be used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT	transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for	response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the	invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., Int J Biochem Cell Biol 51(10):1221-1236 (1999); Ali et al., Int.	at., J. Immunol 105(12).7213-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the

disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-
contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT
	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).
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response element that may be	mediated immune response.
used or routinely modified to	Additional highly preferred
test NFAT-response element	indications include
 activity of polypeptides of the	inflammation and inflammatory
invention (including antibodies	disorders. An additional highly
and agonists or antagonists of	preferred indication is infection
the invention) include assays	(e.g., an infectious disease as
disclosed in Berger et al., Gene	described below under
66:1-10 (1998); Cullen and	"Infectious Disease").
Malm, Methods in Enzymol	Preferred indications include
216:362-368 (1992); Henthorn	neoplastic diseases (e.g.,
et al., Proc Natl Acad Sci USA	leukemia, lymphoma, and/or as
85:6342-6346 (1988);	described below under
Aramburu et al., J Exp Med	"Hyperproliferative Disorders").
182(3):801-810 (1995); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	neoplasms and cancers, such as,
31(10):1221-1236 (1999);	for example, leukemia,
Fraser et al., Eur J Immunol	lymphoma, and prostate, breast,
 29(3):838-844 (1999); and	lung, colon, pancreatic,
Yeseen et al., J Biol Chem	esophageal, stomach, brain,
268(19):14285-14293 (1993),	liver and urinary cancer. Other
the contents of each of which	preferred indications include
are herein incorporated by	benign dysproliferative
 reference in its entirety. NK	disorders and pre-neoplastic
cells that may be used according	conditions, such as, for example,
to these assays are publicly	hyperplasia, metaplasia, and/or
available (e.g., through the	dysplasia. Preferred
ATCC). Exemplary human NK	indications also include anemia,
cells that may be used according	pancytopenia, leukopenia,
to these assays include the NK-	thrombocytopenia, Hodgkin's
YT cell line, which is a human	disease, acute lymphocytic
natural killer cell line with	anemia (ALL), plasmacytomas,
cytolytic and cytotoxic activity.	multiple myeloma, Burkitt's

lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred	indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms		liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example,
antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	Methods in Enzymol 210:302-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862- 3873 (1994); and Black et al., Virus Genes 12(2):105-117	which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell	killer cell line with cytolytic and cytotoxic activity.	

hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia,	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's	disease, acute lymphocytic anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophinia, psoriasis, suppression of	immune reactions to	transplanted organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication is	infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Highly preferred indications	such as, for example, leukemia,	
																		Assays for the activation of	transcription through the	Gamma Interferon Activation	Site (GAS) response element are	well-known in the art and may	be used or routinely modified to	assess the ability of	polypepuaes of the interior
																		Activation of	transcription through	GAS response	element in immune	cells (such as T-	cells).		
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																		HRXCX15							
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lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease),	melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include henion dysproliferative	disorders and pre-neoplastic conditions, such as, for example,	hyperplasia, metaplasia, and/or dysplasia. Preferred indications	include autoimmune diseases	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune response,	and suppressing a T cell-	mediated immune response.	Additional preferred indications include inflammation and	inflammatory disorders. Highly	preferred indications include	blood disorders (e.g., as	described below under "Immune		Disorders", and/or	"Cardiovascular Disorders"),
(including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and	modulate gene expression involved in a wide variety of cell finctions. Exemplary	assays for transcription through the GAS response element that	modified to test GAS-response element activity of polypeptides	of the invention (including antibodies and agonists or	antagonists of the invention)	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol 155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by reference	in its entirety. Exemplary	human T cells, such as the	SUPT cell line, that may be used	according to these assays are	publicly available (e.g., through
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and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes meningitis, Lyme Disease, and asthma and allergy.	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as
and infection (e.g., viral infections, tuberculosis, infections associated wirchronic granulomatosus and malignant osteoport and/or an infectious dise described below under "Infectious Disease"). A additional preferred indicipathic pulmonary fill Preferred indications in anemia, pancytopenia, leukopenia, thrombocyt acute lymphocytic anem (ALL), plasmacytomas, myeloma, arthritis, AID granulomatory bowel disease, inflammatory bowel disease, inflammatory bowel diseases, neutrophilia, psoriasis, suppression of immune reactions to transplante and tissues, hemophilis, hypercoagulation, diabe mellitus, endocarditis, meningitis, Lyme Disea asthma and allergy.	Highly prefinctude aller Additional Pindications in hematopoiet
the ATCC).	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of
	Production of IL-10 and activation of T-cells.
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		nolvnentides of the invention	described below under minimizer
		(including antibodies and	Activity", and "Blood-Related
		agonists or antagonists of the	Disorders"), autoimmune
		invention) to stimulate or inhibit	diseases (e.g., rheumatoid
	8.	production of IL-10 and/or	arthritis, systemic lupus
		activation of T-cells.	erythematosis, Crohn's disease,
		Exemplary assays that may be	multiple sclerosis and/or as
•		used or routinely modified to	described below),
		assess the ability of	immunodeficiencies (e.g., as
		polypeptides and antibodies of	described below), boosting a T
	1	the invention (including agonists	cell-mediated immune response,
		or antagonists of the invention)	and suppressing a T cell-
-		to modulate IL-10 production	mediated immune response.
		and/or T-cell proliferation	
		include, for example, assays	
		such as disclosed and/or cited	
		in: Robinson, DS, et al., "Th-2	
		cytokines in allergic disease" Br	
		Med Bull; 56 (4): 956-968	
		(2000), and Cohn, et al., "T-	
		helper type 2 cell-directed	
		therapy for asthma"	
		Pharmacology & Therapeutics;	
		88: 187-196 (2000); the contents	
		of each of which are herein	
		incorporated by reference in	
		their entirety. Exemplary cells	
		that may be used according to	-
		these assays include Th2 cells.	
		IL10 secreted from Th2 cells	
		may be measured as a marker of	
		Th2 cell activation. Th2 cells	
		are a class of T cells that secrete	

	Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications also include cancers such as, kidney, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, urinary cancer, lymphoma and leukemias. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease,	acute lymphocytic anemia
	Highly pre include ne as describ "Hyperpre Highly pre also include, moreast, lure esophages liver, urin and leuken indication dysprolife pre-neoplife pre-neoplif	acute lym
IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours. LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al.,	Circ Res, 89(8):732-39 (2001),
	Activation of Transcription	
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Discurdances and low "Dlood	Disolucis, allu/ol Bioou-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity") and infections (e.g.,	as described below under	"Infectious Disease").	Preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary cancer, lymphoma	and leukemias. Other preferred	indications include benign	dysproliferative disorders and
IM Dischar Con Sum 64:00	Jivi, Biochem Soc Symp 04:29-	48 (1999); Chang and Karin,	Nature 410(6824):37-40 (2001);	and Cobb MH, Prog Biophys	Mol Biol 71(3-4):479-500	(1999); the contents of each of	which are herein incorporated	by reference in its entirety.	Natural killer cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC). Exemplary	natural killer cells that may be	used according to these assays	include the human natural killer	cell lines (for example, NK-YT	cells which have cytolytic and	cytotoxic activity) or primary	NK cells.														
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pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS,	inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications
		Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through
		Activation of transcription through serum response element in immune cells (such as natural killer cells).
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include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include		leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,		malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,
the SRE that may be used or routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson et	al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary T cells that	may be used according to these	assays include the NK-YT cell	line, which is a human natural	killer cell line with cytolytic and	cytotoxic activity.				
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preferred indications include	benign dysproliterative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophilia,	psoriasis, suppression of	immune reactions to	transplanted organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication is	infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Preferred embodiments of the	invention include using	polypeptides of the invention (or	antibodies, agonists, or
								-				-																Caspase Apoptosis. Assays for	caspase apoptosis are well	known in the art and may be	used or routinely modified to
				-														•										Regulation of	apoptosis of immune	cells (such as mast	cells).
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antagonists thereof) in detection,	diagnosis, prevention, and/or	treatment of asthma, allergy,	hypersensitivity and	inflammation.																												
assess the ability of	nolvnentides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate caspase	protease-mediated apoptosis in	immune cells (such as, for	example, in mast cells). Mast	cells are found in connective	and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -antigen,	promoted by T helper cell type 2	cytokines, is an important	component of allergic disease.	Dysregulation of mast cell	apoptosis may play a role in	allergic disease and mast cell	tumor survival. Exemplary	assays for caspase apoptosis that	may be used or routinely	modified to test capase	apoptosis activity induced by	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in: Masuda A, et al., J	Biol Chem, 276(28):26107-	26113 (2001); Yeatman CF 2nd,	et al., J Exp Med, 192(8):1093-	1103 (2000);Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);

Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
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of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells.	such assays that they or used of routinely modified to test immunomodulatory activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) include the assays disclosed in Miraglia et al., J	Biomolecular Screening 4:193-204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Coccni et al., Science 270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	through the ATCC). Exemplary	endothelial cells that may be	used according to these assays	include human umbilical vein	endothelial cells (HUVEC),	which are endothelial cells	which line venous blood vessels,	and are involved in functions
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			that include, but are not limited to, angiogenesis, vascular	
			permeability, vascular tone, and immune cell extravasation.	
HCEEE79	472	Production of IL-10	Assays for production of IL-10	Highly preferred indications include allergy and asthma.
		cells.	well known in the art and may	Additional highly preferred
			be used or routinely modified to	indications include immune and
			assess the ability of	hematopoietic disorders (e.g., as
			polypeptides of the invention	described below under "Immune
			(including antibodies and	Activity", and "Blood-Related
			agonists or antagonists of the	Disorders"), autoimmune
			invention) to stimulate or inhibit	diseases (e.g., rheumatoid
	•		production of IL-10 and/or	arthritis, systemic lupus
			activation of T-cells.	erythematosis, Crohn's disease,
			Exemplary assays that may be	multiple sclerosis and/or as
			used or routinely modified to	described below),
	-		assess the ability of	immunodeficiencies (e.g., as
			polypeptides and antibodies of	described below), boosting a T
			the invention (including agonists	cell-mediated immune response,
			or antagonists of the invention)	and suppressing a T cell-
			to modulate IL-10 production	mediated immune response.
			and/or T-cell proliferation	
			include, for example, assays	
			such as disclosed and/or cited	
			in: Robinson, DS, et al., "Th-2	
			cytokines in allergic disease" Br	
	-		Med Bull; 56 (4): 956-968	
	_		(2000), and Cohn, et al., "T-	
			helper type 2 cell-directed	
			therapy for asthma"	
			Pharmacology & Therapeutics;	

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as
88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate
	Activation of transcription through serum response element in immune cells (such as Tecells).
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described below under "Immune Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	meianoma, gnoma (v.5.,
the expression of genes involved in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SKE	activity of the polypopulates of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and Black	et al., Virus Genes 12(2):105-	117 (1997), the content of each	of which are herein incorporated	by reference in its entirety. T	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary mouse T	cells that may be used according	to these assays include the	CTLL cell line, which is an IL-2	dependent suspension culture of	T cells with cytotoxic activity.				
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malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esonhageal stomach brain.	liver and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred	indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's	disease, acute lymphocytic anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease,	inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to	transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,	cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is	infection (e.g., an infectious disease as described below under "Infectious Disease").

A highly preferred embodiment of the invention	includes a method for inhibiting	(e.g., decreasing) The alpina	highly preferred embodiment of	the invention includes a method	for stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred
A higl embodin	includes	e.g., de	highly p	the inve	for stim	TNF alp	Highly p	include	describe	Activity	Disorde	"Cardio	Highly	include	(e.g., rh	systemi	Crohn"s	sclerosi	below),	(e.g., as	boostin	immun	suppres	immun	highly	include	inflamr	treating	with rh	additio
TNFa FMAT. Assays for immunomodulatory proteins	produced by activated	macrophages, I cells,	other cell types that exert a wide	variety of inflammatory and	cytotoxic effects on a variety of	cells are well known in the art	and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, modulate	inflammation and cytotoxicity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or cytotoxic	response. Such assays that may	be used or routinely modified to	test immunomodulatory activity	of polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-
Production of TNF alpha by dendritic	cells									_																				
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	204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	indication is sepsis. Highly preferred indications include neoplastic diseases (e.g.,
	(2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol	leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders").
	160(7):3585-3593 (1998); Verhasselt et al J Immunol	Additionally, highly preferred indications include neoplasms
	158:2919-2925 (1997); and	and cancers, such as, leukemia,
	Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents	(e.g., malignant glioma), solid
	of each of which are herein	tumors, and prostate, breast,
•	incorporated by reference in its	lung, colon, pancreatic,
	that may be used according to	liver and urinary cancer. Other
	these assays may be isolated	preferred indications include
	using techniques disclosed	benign dysproliferative
	herein or otherwise known in	disorders and pre-neoplastic
	the art. Human dendritic cells	conditions, such as, for example,
	are antigen presenting cells in	hyperplasia, metaplasia, and/or
	suspension culture, which, when	dysplasia. Preferred
	activated by antigen and/or	indications include anemia,
	cytokines, initiate and	pancytopenia, leukopenia,
	upregulate T cell proliferation	thrombocytopenia, Hodgkin's
	and functional activities.	disease, acute lymphocytic
		anemia (ALL), plasmacytomas,
		multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		neutropenia, neutrophilia,
	-	psoriasis, suppression of
		immune reactions to

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transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for inhibiting adipocyte activation. An adipocyte activation. An adipocyte activation. An adipocyte activation. An	alternative highly preferred
	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	include the assays disclosed in
	Activation of Adipocyte ERK Signaling Pathway	
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embodiment of the invention	includes a method for inhibiting	the activation of (e.g.,	decreasing) and/or inactivating	adipocytes. Highly	preferred indications include	endocrine disorders (e.g., as	described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic diseases	(e.g., lipomas, liposarcomas,	and/or as described below under	"Hyperproliferative Disorders").	Preferred indications include	blood disorders (e.g.,	hypertension, congestive heart	failure, blood vessel blockage,	heart disease, stroke, impotence	and/or as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as described	below under "Infectious	Disease). preferred indication is diabetes
emt	incl	the	dec	adil	pre	end	des	ם	Hig	also	(e.g	anc	H.,	Pre	plo	hy	fai						Ö	<u>e</u>	"Ir	dis	pe			<u>ع</u> هـ	<u> </u>
Forrer et al Biol Chem 379(8-	9):1101-1110 (1998); Le	Marchand-Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety. Mouse	adipocyte cells that may be used	according to these assays are	nublicly available (e.g., through	the ATCC). Exemplary mouse	adipocyte cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1 is	an adherent mouse preadipocyte	cell line that is a continuous	substrain of 3T3 fibroblast cells	developed through clonal	isolation and undergo a pre-	adipocyte to adipose-like	conversion under appropriate	differentiation conditions known	in the art.		
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mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic	retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section	below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion drowsiness	nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the	"Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic
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retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract	and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred	indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional	highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast,

m a vr dy ni ii; ni s tr ni y c	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune ys described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or
	Activation of transcription through serum response element in immune cells (such as T-cells).
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Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below),	immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications	include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred	preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under	"Hyperprollerative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid	tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic
antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	Methods in Enzymol 210:302-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-	of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly	available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2	dependent suspension culture of T cells with cytotoxic activity.	

conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces
	Production of IL-6
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expression of IL-6 has been A flegibly preferred indication is linked to autoimmune disease, highly preferred indication is inhed to autoimmune disease. Assays for diseases. Assays for disease, highly preferred indications include disease, highly preferred indications include disease, highly regulated by a large variety of cells where the expression level cytokines, growth factors, and homones are well known in the homones are well known in the modified to assess the ability of diseases (e.g., as described at and may be used or routinely indication (e.g., as described at and may be used or routinely indications include autoimmune modified to assess the ability of diseases (e.g., as described elementation) to mediate immunomodulation and modulate of the invention of cells with the profileration and modulate of the invention of cells with the profileration and modulate of the Highly preferred indications and immunomodulation and upregulation of include boosting a Berell mannomodulation and upregulation of include boosting a Berell mannomodulation and inflammation and inflammation and inflammation and inflammation and inflammation include indications include countries of the assays that may be used or counting problems and include indications include countries and a says that may be used or counting of include diagrams include indications include countries and inflammation and include indications include countries and inflammation and inflammation and inflammation and inflammation and inflammation indications include countries and inflammation indications are included inflammatical and inflammatical																																	_
expression of IL-6 has been inked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) checking antibodies and differentiation and modulate T cell proliferation and modulate or evokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and upregulation of assays that may be used or routinely modified to test immunomodulatory and differentiation and assays that may be used or routinely modified to test immunomodulatory and differentiation and activities.	(e.g., reducing) IL-6 production.	A highly preferred indication is	the stimulation or enhancement	of mucosal immunity. Highly	preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as described	below under "Infectious	Disease"). Highly preferred	indications include autoimmune	diseases (e.g., rheumatoid	arthritis, systemic lupus	erythematosis, multiple sclerosis	and/or as described below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response and	alternatively suppressing a B	cell-mediated immune response.	Highly preferred indications	include inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,
	cytotoxic T cells. Deregulated	expression of IL-6 has been	linked to autoimmune disease,	plasmacytomas, myelomas, and	chronic hyperproliferative	diseases. Assays for	immunomodulatory and	differentiation factor proteins	produced by a large variety of	cells where the expression level	is strongly regulated by	cytokines, growth factors, and	hormones are well known in the	art and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and the	stimulation and upregulation of	T cell proliferation and	functional activities. Such	assays that may be used or	routinely modified to test	immunomodulatory and	diffferentiation activity of
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myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described	below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms	and cancers, such as, myeloma,	lymphoma, melanoma, and	prostate, oreast, iung, colon, pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Uther preferred indications include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include anemia, pancytopenia,	leukopenia, thrombocytopenia,		lymphocytic anemia (ALL), tinle myeloma Burkitt's	Indiciple injections, Barrier 5 Ivmphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,
polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204(1999); Rowland et al.,	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated hy reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which, when	activated by antigen and/or	upregulate T cell proliferation	and functional activities.					-		
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meningitis, and Lyme Disease. An additional preferred	indication is infection (e.g., an	infections disease as described	below under "Infectious	Disease").	10 Highly preferred indications	include allergy and asthma.		d to indications include immune and	-	described below under "Immune	Activity", and "Blood-Related	Disorders"), autoimmune	nibit diseases (e.g., rheumatoid		erythematosis, Crohn's disease,				of described below), boosting a T			n mediated immune response.			pa	1-2	"Br			
					Assays for production of IL-10	and activation of T-cells are	well known in the art and may	be used or routinely modified to	assess the ability of	nolyneptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate or inhibit	production of IL-10 and/or	activation of T-cells.	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including agonists	or antagonists of the invention)	to modulate IL-10 production	and/or T-cell proliferation	include, for example, assays	such as disclosed and/or cited	in: Robinson, DS, et al., "Th-2	cytokines in allergic disease" Br	Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed
					Production of IL-10	and activation of T-	cells	· Curo																						
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					11000700	HCEFE82																			-					
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	Diabetes A highly preferred indication is diabetes. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the
therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incomorated by reference in its
	Inhibition of squalene synthetase gene transcription.
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	HCEGG08
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"Renal Disorders" section below),	ly, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, near	disease, stroke, impotence (e.g.,	due to diabetic neuropathy or	blood vessel blockage), seizures,	mental confusion, drowsiness,	lycemic-	ъ,	cardiovascular disease (e.g., heart	erosis,	ease,	hypertension, stroke, and other	ders as	described in the "Cardiovascular	n below),	dyslipidemia, endocrine disorders	(as described in the "Endocrine	n below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the urinary	tract and skin). Highly preferred	indications also include obesity,	weight gain, and weight loss, as	well as complications associated	oht oain
isorders"	diabetic neuropathy, nerve	nd nerve	abetic neu	ssel block	stroke, im	abetic ne	ssel block	onfusion,	nonketotic hyperglycemic-	hyperosmolar coma	scular dis	disease, atherosclerosis,	microvascular disease,	ision, stro	diseases and disorders as	d in the "	Disorders" section below),	emia, end	ribed in th	Disorders" section below),	thy, vision	abetic reti	ss), ulcers	nealing, a	fectious d	s as desci	ous Disea	especially	d skin). F	ons also i	gain, and	complica	with obesity weight gain and
"Renal D	diabetic 1	disease a	due to di	plood ve	disease,	due to di	blood ve	mental c	nonketot	hyperosr	cardiova	disease,	microva	hyperten	diseases	describe	Disorder	dyslipid	(as desci	Disorder	neuropa	(e.g., dia	blindnes	wound	(e.g., in	disorder	"Infection	below, 6	tract and	indication	weight	well as	with oh
in its	ed with	AP	er 72		cell	9	3	440	uents	porated	÷																						
incorporated by reference in its	entirety. Cells were treated with	SID supernatants, and SEAP	activity was measured after 72	hours. HepG2 is a human	benatocellular carcinoma cell	11:20 (ATCC HB-8065) See	-ovoy). L		209:49/-9 (1980), the contents	of which are herein incorporated	by reference in its entirety.																						
rated by	Cells w	ernatant	was mea	HepG2 is	elliilar og			Knowies et al., Science.	1861) 6-/	h are her	rence in i																						
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weight loss. Preferred	include methods of preventing,	detecting, diagnosing, treating	and/or ameliorating the above	mentioned conditions, disorders,	and diseases.	Highly preferred indications	include inflammation (acute and	chronic), restnosis,	atherosclerosis, asthma and	allergy. Highly preferred	indications include	inflammation and inflammatory	disorders, immunological	disorders, neoplastic disorders	(e.g. cancer/tumorigenesis), and	cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell carcinoma,	and prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Other preferred indications	include benign dysproliferative
						Assays for measuring	expression of VCAM are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate VCAM	expression. For example,	FMAT may be used to meaure	the upregulation of cell surface	VCAM-1 expression in	endothelial cells. Endothelial	cells are cells that line blood	vessels, and are involved in	functions that include, but are	not limited to, angiogenesis,	vascular permeability, vascular	tone, and immune cell	extravasation. Exemplary	endothelial cells that may be	used according to these assays	include human umbilical vein	endothelial cells (HUVEC),	which are available from
						Production of	VCAM in	endothelial cells	(such as human	umbilical vein	endothelial cells	(HIIVEC))									-						_				
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disorders and pre-neopiastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,
commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular factors can cause an influx of calcium, leading to activation of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions.
	Stimulation of Calcium Flux in pancreatic beta cells.
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nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract	and skin), carpal tunnel	syndrome and Dupuytren's	contracture). An additional	highly preferred indication is	obesity and/or complications	associated with obesity.	Additional highly preferred	indications include weight loss	or alternatively, weight gain.	Aditional highly preferred	indications are complications	associated with insulin
used or routinely modified to	measure calcium flux by	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in: Satin LS, et al.,	Endocrinology, 136(10):4589-	601 (1995);Mogami H, et al.,	Endocrinology, 136(7):2960-6	(1995); Richardson SB, et al.,	Biochem J, 288 (Pt 3):847-51	(1992); and, Meats, JE, et al.,	Cell Calcium 1989 Nov-	Dec;10(8):535-41 (1989), the	contents of each of which is	herein incorporated by reference	in its entirety. Pancreatic cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be routinely	generated. Exemplary	pancreatic cells that may be	used according to these assays	include HITT15 Cells. HITT15	are an adherent epithelial cell	line established from Syrian	hamster islet cells transformed	with SV40. These cells express	glucagon, somatostatin, and	glucocorticoid receptors. The	cells secrete insulin, which is
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resistance.	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders.	.≛∖
stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene
	Activation of transcription through cAMP response element in immune cells (such as Tcells).	
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diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma,	Hodgkin"s disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia,	pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia.
66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated	by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the HTZ cell line, which is a suspension culture of IL-2 dependent T cells that also respond to IL-4.	
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					hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
63	HCFLN88	477	Activation of transcription through serum response element in immune cells (such as Tells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and
				85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-	immune response. Additional highly preferred indications

disorders	damage in pat oid arthritis.	damage in pativida arthritis. A hly preferred epsis. Highl cations include	damage in patie bid arthritis. Ar hly preferred epsis. Highly cations include eases (e.g., phoma, and/or	damage in patien bid arthritis. An hly preferred epsis. Highly cations include eases (e.g., phoma, and/or ander rative Disorders highly preferred	damage in patien bid arthritis. An hly preferred epsis. Highly cations include eases (e.g., phoma, and/or ow under rative Disorders highly preferred clude neoplasms	damage in patien bid arthritis. An hly preferred epsis. Highly cations include eases (e.g., uphoma, and/or ander rative Disorders highly preferrectlude neoplasms uch as, for	damage in patier damage in patier bid arthritis. An hly preferred epsis. Highly cations include eases (e.g., phoma, and/or rative Disorders highly preferred clude neoplasms uch as, for emia, lymphomagans (e.g., emia, lymphomagans)	damage in patien bid arthritis. An hly preferred epsis. 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Other cations include pre-neoplastic ch as, for example netaplasia, and/or restared clude anemia, leukopenia, leukopenia,	reating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders") Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, Hodgkin's thrombocytopenia, Hodgkin's	damage in patient damage in patient bid arthritis. An hly preferred epsis. 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Virus Genes 12(2):105-117 (1997), the content of each of	are nerein incorpa	which are nerein incorporated by reference in its entirety. Mouse T cells that may be used according to these assays are	which are herein incorporated by reference in its entirety. Mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used	which are herein incorport by reference in its entirety. Mouse T cells that may be according to these assays publicly available (e.g., the ATCC). Exemplary in T cells that may be used according to these assays include the HT2 cell line.	which are herein incorporated by reference in its entirety. Mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is an IL-2 dependent suspension	which are herein incorporated by reference in its entirety. Mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is an IL-2 dependent suspension culture of T cells that also	are nerein incorportence in its entire rence in its entire. T cells that may ing to these assay y available (e.g., CC). Exemplary that may be used ing to these assay of the HT2 cell line. 2 dependent sus of T cells that all to IL-4.	are nerein incorportence in its entire rence in its entire. T cells that may ing to these assay y available (e.g., CC). Exemplary that may be used ing to these assay of the HT2 cell line. 2-2 dependent sus of T cells that all to IL-4.	are nerein incorportering to these assay ing to these assay y available (e.g., CC). Exemplary that may be used ing to these assay in the HT2 cell line and to the that also of T cells that also of T cells that also it to IL-4.	are nerein incorporter frence in its entire. T cells that may ing to these assay available (e.g., CC). Exemplary that may be used ing to these assay in the HT2 cell ling. -2 dependent sus of T cells that all to IL-4.	are nerein incorportence in its entire rence in its entire. T cells that may ing to these assay y available (e.g., CC). Exemplary that may be used ing to these assay in the HT2 cell line2 dependent sus of T cells that all to IL-4.	are nerein incorportence in its entire rence in its entire. T cells that may ing to these assay y available (e.g., CC). Exemplary that may be used ing to these assay is the HT2 cell line. J. dependent sus of T cells that all d to IL-4.	are nerein incorporter frence in its entire rence in its entire T cells that may ing to these assay available (e.g., CC). Exemplary that may be used ing to these assay the HT2 cell ling to the that all to IL-4.	are nerein incorporter of the control of the contro	are nerein incorpore rence in its entire rence in its entire. T cells that may ing to these assay y available (e.g., CC). Exemplary that may be used ing to these assay is the HT2 cell line. Jet dependent sus of T cells that all to IL-4.	are nerein incorpore rence in its entire rence in its entire. T cells that may ing to these assay y available (e.g., CC). Exemplary that may be used ing to these assay is the HT2 cell ling to these assay of T cells that all to IL-4.	are nerein incorporter frence in its entire rence in its entire. T cells that may mg to these assay y available (e.g., CC). Exemplary that may be used ing to these assay the HT2 cell ling to these assay of T cells that also to IL-4.	are nerein incorporter of the control of the contro	are nerein incorporter of the sentite of the sentite of the sent o	are nerein incorporter of the sentire frence in its entire. The cells that may available (e.g., CC). Exemplary that may be used ing to these assay in the HT2 cell ling to these assay of T cells that all to IL-4.	are nerein incorporter frence in its entire rence in its entire T cells that may mg to these assay y available (e.g., CC). Exemplary that may be used ing to these assay the HT2 cell line of T cells that all to IL-4.	are nerein incorpore rence in its entire rence in its entire T cells that may ing to these assay y available (e.g., CC). Exemplary that may be used ing to these assay is the HT2 cell line of T cells that all d to IL-4.
(1997), the content of each of which are herein incorporated	٠.	by reference I Mouse T cells according to	by reference Mouse T cell: according to publicly avail the ATCC). I	by reference Mouse T cell according to t publicly avail the ATCC). T cells that m according to t	by reference Mouse T cells according to t publicly avail the ATCC). T cells that m according to include the H	by reference Mouse T cells according to the publicly avail the ATCC). I T cells that m according to include the H is an IL-2 dep	by reference in I Mouse T cells the according to the publicly availab. The ATCC). Exe T cells that may according to the include the HT2 is an IL-2 depenculture of T cells respond to IL-4.	by reference Mouse T cells according to the ATCC). I T cells that m according to the H include the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to to publicly avail the ATCC). I T cells that m according to include the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to the ATCC). It cells that maccording to the ATCC). It cells that maccording to the His an IL-2 depending to the His an IL-2 dependent of T cellure of T cellure of T cellure of T cellure.	by reference Mouse T cells according to the ATCC). I T cells that m according to the H is an IL-2 deg culture of T c respond to IL	by reference Mouse T cells according to the ATCC). I T cells that m according to tinclude the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to the ATCC). T T cells that m according to the H include the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to the ATCC). It cells that maccording to the ATCC) is an IL-2 dependence of T cellure of T cellur	by reference Mouse T cells according to the ATCC). I T cells that m according to tinclude the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to the ATCC). I T cells that m according to the H include the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to the ATCC). T T cells that m according to the H include the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to the ATCC). I T cells that m according to tinclude the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to to publicly avail the ATCC). I T cells that m according to to include the H is an IL-2 dep culture of T c respond to IL	by reference Mouse T cells according to the ATCC). T cells that m according to the include the H is an IL-2 depending to IL-2 dependence of T cells that m according to the maccording to the H is an IL-2 dependence of T cells that m according to the H is an IL-2 dependence of T cells that m according to the include the H is an IL-2 dependence of T cells that m include the IL-2 dependence of T cells that m include the IL-2 dependence of T cells that m include the IL-2 dependence of T cells that m include the IL-2 dependence of T cells that m include the IL-2 dependence of T cells that m include the IL-2 dependence of T cells that m include the IL-2 dependence of T cells that m include the IL-2 dependence of T cells that m include the III-2 dependence of T cells that m include the II-2 dependence	by reference Mouse T cells according to 1 publicly avail the ATCC). T cells that m according to 1 include the H is an IL-2 dep culture of T c respond to IL.	by reference Mouse T cells according to the ATCC). In the ATCC). The Cells that maccording to the Hear is an IL-2 dependence of T cells that the is an IL-2 dependence of T cells the Hear is an IL-2 dependence of T cells the Hear is an IL-2 dependence of T cells the Hear III and III are spond to IL tespond to
Vir (19) whi	_	by 1 Mo	Mo Mo acc pub the T c	Mo Mo acc T c acc	Mo accomply 1 by 1	Mo acc pub the the acc acc incl is a	Mo acc pub the the T c acc acc acc incl incl is a cult	Mo acc acc by 1 T c acc acc acc acc acc acc acc c acc c acc c acc c acc ac	Mo acc acc acc by 1 bub bub the the the incl incl is a cult rest	Mo According to the Conference of the Conference	Mo acc acc acc acc acc acc acc acc acc ac	Mo account the the inclusive cult response in the cult response inclusive cult response inclusive cult account response inclusive cult account response inclusive cult account response inclusive cult response inclusive cult	Mo Ago Ago Ago Ago Ago Ago Ago Ago Ago Ag	Mo acc acc acc acc acc acc acc acc acc ac	Mo account the pub pub pub the incl is a count rest rest	Mo Aforest	Mo Ago Ago Ago Ago Ago Ago Ago Ago Ago Ag	Mo acc acc acc acc acc acc acc acc acc ac	Mo Mo according the pub pub pub the incl is a coll is a coll is a coll is a coll incl incl is a coll incl incl incl incl incl incl incl in	Mo M	Mo M	Mo Mo account the the incl is a count incl incl is a count incl incl is a count incl incl incl incl incl incl incl incl
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lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Immune Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving T-cells).
	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively
	cells
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	HCFLT90
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on CD4+ and CD8+ T cells are	well known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to modulate the	activation of T cells, maintain	T cell homeostasis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the upregulation of	cell surface markers, such as	CD152, and the activation of T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include, for	example, the assays disclosed	in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); McCoy et al., Immunol
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			Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated	
HCRAY10	480	Production of IFNgamma using a T cells	by reference in its entirety. IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infections, tuberculosis,

chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly	preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiency (e.g.,	as described below), boosting a T cell-mediated immune response, and suppressing a T	cell-mediated immune response. Additional highly preferred indications include	inflammation and inflammatory disorders. Additional preferred	indications include idiopathic pulmonary fibrosis. Highly preferred indications include	neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described	below under "Hyperproliferative Disorders"), Highly preferred	indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,	melanoma, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	immunomodulation, regulate inflammatory activities, modulate TH2 helper cell	function, and/or mediate humoral or cell-mediated immunity. Exemplary assays	that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon	gamma (IFNg), and the activation of T cells. Such assays that may be used or	routinely modified to test immunomodulatory activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include the assays disclosed in Miraglia et al., J	204 (1999); Rowland et al., "Lymphocytes: a practical	approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al.,	Annu Rev Immunol 15:749-795 (1997), and Rheumatology
											
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				(Oxford) 38(3):214-20 (1999)	nreferred indications include
				the contents of each of which	benign dysproliferative
				are herein incorporated by	disorders and pre-neoplastic
				reference in its entirety. Human	conditions, such as, for example,
				T cells that may be used	hyperplasia, metaplasia, and/or
				according to these assays may	dysplasia. Preferred
				be isolated using techniques	indications include anemia,
				disclosed herein or otherwise	pancytopenia, leukopenia,
				known in the art. Human T	thrombocytopenia, Hodgkin's
				cells are primary human	disease, acute lymphocytic
				lymphocytes that mature in the	anemia (ALL), plasmacytomas,
				thymus and express a T Cell	multiple myeloma, Burkitt's
				receptor and CD3, CD4, or	lymphoma, arthritis, AIDS,
				CD8. These cells mediate	granulomatous disease,
				humoral or cell-mediated	inflammatory bowel disease,
				immunity and may be	sepsis, neutropenia,
				preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted organs
_					and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HCRBF72	481	Activation of	Assays for the activation of	Highly preferred indications
29			transcription through	transcription through the	include neoplastic diseases (e.g.,
			GAS response	Gamma Interferon Activation	Ieukemia, lymphoma, and/or as
			element in immune	Site (GAS) response element are	described below under
			cells (such as T-	well-known in the art and may	"Hyperproliferative Disorders").
			cells).	be used or routinely modified to	Highly preferred indications
				assess the ability of	include neoplasms and cancers,
				polypeptides of the invention	such as, for example, leukemia,

	(including antibodies and	Ivmohoma (e.g., T cell
	agonists or antagonists of the	lymphoma, Burkitt's
	invention) to regulate STAT	lymphoma, non-Hodgkins
	transcription factors and	lymphoma, Hodgkin"s disease),
	modulate gene expression	melanoma, and prostate, breast,
	involved in a wide variety of	lung, colon, pancreatic,
	cell functions. Exemplary	esophageal, stomach, brain,
	assays for transcription through	liver and urinary cancer. Other
	the GAS response element that	preferred indications include
	may be used or routinely	benign dysproliferative
	modified to test GAS-response	disorders and pre-neoplastic
	element activity of polypeptides	conditions, such as, for example,
	of the invention (including	hyperplasia, metaplasia, and/or
	antibodies and agonists or	dysplasia. Preferred indications
	antagonists of the invention)	include autoimmune diseases
	include assays disclosed in	(e.g., rheumatoid arthritis,
	Berger et al., Gene 66:1-10	systemic lupus erythematosis,
	(1998); Cullen and Malm,	multiple sclerosis and/or as
	Methods in Enzymol 216:362-	described below),
	368 (1992); Henthorn et al.,	immunodeficiencies (e.g., as
	Proc Natl Acad Sci USA	described below), boosting a T
	85:6342-6346 (1988);	cell-mediated immune response,
	Matikainen et al., Blood	and suppressing a T cell-
	93(6):1980-1991 (1999); and	mediated immune response.
	Henttinen et al., J Immunol	Additional preferred indications
	155(10):4582-4587 (1995), the	include inflammation and
	contents of each of which are	inflammatory disorders. Highly
	herein incorporated by reference	preferred indications include
	in its entirety. Exemplary	blood disorders (e.g., as
	human T cells, such as the	
	SUPT cell line, that may be used	
`	according to these assays are	Disorders", and/or
	publicly available (e.g., through	"Cardiovascular Disorders"),

and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred
the ATCC).	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production
	Production of IL-6
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	HCRNF78
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	 (1gA piays a fole III inucosai	includes a method for inhibiting
	 immunity). IL-6 induces	includes a memod for minorung
	cytotoxic T cells. Deregulated	(e.g., reducing) IL-6 production.
	expression of IL-6 has been	A highly preferrred indication is
	linked to autoimmune disease,	the stimulation or enhancement
-	plasmacytomas, myelomas, and	of mucosal immunity. Highly
	chronic hyperproliferative	preferred indications include
	diseases. Assays for	blood disorders (e.g., as
	immunomodulatory and	described below under "Immune
	differentiation factor proteins	Activity", "Blood-Related
	produced by a large variety of	Disorders", and/or
	cells where the expression level	"Cardiovascular Disorders"),
	 is strongly regulated by	and infection (e.g., as described
	 cytokines, growth factors, and	below under "Infectious
	hormones are well known in the	Disease"). Highly preferred
	art and may be used or routinely	indications include autoimmune
	modified to assess the ability of	diseases (e.g., rheumatoid
	polypeptides of the invention	arthritis, systemic lupus
	(including antibodies and	erythematosis, multiple sclerosis
	agonists or antagonists of the	and/or as described below) and
	invention) to mediate	immunodeficiencies (e.g., as
	immunomodulation and	described below). Highly
	differentiation and modulate T	preferred indications also
	 cell proliferation and function.	include boosting a B cell-
	Exemplary assays that test for	mediated immune response and
- 40	immunomodulatory proteins	alternatively suppressing a B
	 evaluate the production of	cell-mediated immune response.
	cytokines, such as IL-6, and the	Highly preferred indications
	stimulation and upregulation of	include inflammation and
	T cell proliferation and	inflammatory
	 functional activities. Such	disorders.Additional highly
	assays that may be used or	preferred indications include
	routinely modified to test	asthma and allergy. Highly

preferred indications include neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,
immunomodulatory and differentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which, when	activated by antigen and/or	cytokines, initiate and	upregulate T cell proliferation	and functional activities.					
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					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
	-				indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HCUAF85	483	Activation of	Assays for the activation of	Preferred embodiments of the
69			transcription through	transcription through the NFKB	invention include using
			NFKB response	response element are well-	polypeptides of the invention (or
			element in epithelial	known in the art and may be	antibodies, agonists, or
			cells (such as HELA	used or routinely modified to	antagonists thereof) in detection,
			cells).	assess the ability of	diagnosis, prevention, and/or
				polypeptides of the invention	treatment of Cancer, Wound
				(including antibodies and	Healing, and Inflamation.
				agonists or antagonists of the	Highly preferred indications
				invention) to regulate NFKB	include neoplastic diseases (e.g.,
				transcription factors and	as described below under
				modulate expression of	"Hyperproliferative Disorders").
				epithhelial genes. Exemplary	Highly preferred indications
				assays for transcription through	include neoplasms and cancers,
				the NFKB response element that	such as, for example, melanoma,
				may be used or routinely	and prostate, breast, lung, colon,
				modified to test NFKB-response	pancreatic, esophageal, stomach,
				element activity of polypeptides	brain, liver and urinary cancer.
				of the invention (including	Other preferred indications
				antibodies and agonists or	include benign dysproliferative
				antagonists of the invention)	disorders and pre-neoplastic
				include assays disclosed in:	conditions, such as, for example,
				Kaltschmidt B, et al., Oncogene,	hyperplasia, metaplasia, and/or
				18(21):3213-3225 (1999); Beetz	dysplasia. Preferred

inflammation and inflammatory disorders.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred
A, et al., Int J Radiat Biol, 76(11):1443-1453 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al., Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the HELA cell line.	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to inhibit caspase
	Protection from Endothelial Cell Apoptosis.
	484
	HCUCF89
	70

embodiment of the invention includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment of	the invention includes a method	for inhibiting endothelial cell	proliferation. A highly	preferred embodiment of the	invention includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method for	inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An alternative	highly preferred embodiment of	the invention includes a method	for inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred embodiment	of the invention includes a	method for stimulating	angiogenisis. An alternative	highly preferred embodiment of	the invention includes a method	for inhibiting angiogenesis.	A highly preferred embodiment	of the invention includes a
protease-mediated apoptosis. Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	caspase apoptosis rescue of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Romeo et al.,	Cardiovasc Res 45(3): 788-794	(2000); Messmer et al., Br J	Pharmacol 127(7): 1633-1640	(1999); and J Atheroscler	Thromb 3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by reference	in its entirety. Endothelial cells	that may be used according to	these assays are publicly	available (e.g., through	commercial sources).	Exemplary endothelial cells that	may be used according to these	assays include bovine aortic	endothelial cells (bAEC), which	are an example of endothelial	cells which line blood vessels	and are involved in functions	that include, but are not limited	to, angiogenesis, vascular	permeability, vascular tone, and	immune cell extravasation.
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											-																				

	method	method for reducing cardiac
	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	only An offernotive
	niyperu 	hyperuopily. All alternative
	nignly	highly preferred embodiment of
	the inve	the invention includes a method
	for ind	for inducing cardiac
	hypertrophy.	ophy. Highly
	preferr	preferred indications include
	neoplas	neoplastic diseases (e.g., as
	describ	described below under
	"Hyper	"Hyperproliferative Disorders"),
	and dis	and disorders of the
	cardiov	cardiovascular system (e.g.,
	heart di	heart disease, congestive heart
	failure,	failure, hypertension, aortic
	stenosis	stenosis, cardiomyopathy,
	valvula	valvular regurgitation, left
	ventric	ventricular dysfunction,
	atheros	atherosclerosis and
_	atheros	atherosclerotic vascular disease,
	diabetic	diabetic nephropathy,
	intracal	intracardiac shunt, cardiac
	hypertr	hypertrophy, myocardial
	infarcti	infarction, chronic
	 hemod	hemodynamic overload, and/or
	as desc	as described below under
	"Cardic	"Cardiovascular Disorders").
	Highly	Highly preferred indications
	 include	include cardiovascular,
	 endothe	endothelial and/or angiogenic
	 disorde	disorders (e.g., systemic
	disorde	disorders that affect vessels such
	as diab	as diabetes mellitus, as well as
	disease	diseases of the vessels

Г																																	
	as of the	arteries, capillaries, veins and/or	ghly preferred	hat stimulate	d/or	ation. Highly	lications that	esis and/or	ation.	l indications	ogenic activity	nors, leukemias,	rcoma, and	. Highly	tions include	ancer, such as,	Kaposi"s sarcoma, hemangioma	ivernous),	telangiectasia,	natosis,	nelioma,		ytoma,		oma. Highly	tions also	such as,	lung, colon,	pancreatic, esophageal, stomach,	urinary cancer.	tions include	ferative	e-neoplastic
1	memserves, such as of the	arteries, capillari	lymphatics). Highly preferred	are indications that stimulate	angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors, leukemias,	and Kaposi"s sarcoma, and	retinal disorders. Highly	preferred indications include	neoplasms and cancer, such as,	Kaposi"s sarcom	(capillary and cavernous),	glomus tumors, telangiectasia,	bacillary angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esop	brain, liver, and urinary cancer.	Preferred indications include	benign dysproliferative	disorders and pre-neoplastic
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almara not no this military	Collections, such as, 101 example,	a, ⊐	dysplasia. Highly preferred	indications also include arterial	disease, such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s disease	and Reynaud"s phenomenom,	aneurysms, restenosis; venous	and lymphatic disorders such as	thrombophlebitis, lymphangitis,	and lymphedema; and other	vascular disorders such as	peripheral vascular disease, and	cancer. Highly preferred	indications also include trauma	such as wounds, burns, and	injured tissue (e.g., vascular	injury such as, injury resulting	from balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke, graft	rejection, diabetic or other	retinopathies, thrombotic and	coagulative disorders,
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	cells (such as mast	known in the art and may be	polypeptides of the invention (or
	cells).	used or routinely modified to	antibodies, agonists, or
		assess the ability of	antagonists thereof) in detection,
		polypeptides of the invention	diagnosis, prevention, and/or
		(including antibodies and	treatment of asthma, allergy,
		agonists or antagonists of the	hypersensitivity and
		invention) to regulate caspase	inflammation.
-		protease-mediated apoptosis in	
		immune cells (such as, for	
		example, in mast cells). Mast	
		cells are found in connective	
	-	and mucosal tissues throughout	
		the body, and their activation	
		via immunoglobulin E -antigen,	
		promoted by T helper cell type 2	
		cytokines, is an important	
		component of allergic disease.	
		Dysregulation of mast cell	
		apoptosis may play a role in	
		allergic disease and mast cell	
		tumor survival. Exemplary	
		assays for caspase apoptosis that	
		may be used or routinely	
		modified to test capase	
		apoptosis activity induced by	
		polypeptides of the invention	
		(including antibodies and	
		agonists or antagonists of the	
		invention) include the assays	
		disclosed in: Masuda A, et al., J	
		Biol Chem, 276(28):26107-	
		26113 (2001); Yeatman CF 2nd,	
		et al., J Exp Med, 192(8):1093-	

·				1103 (2000); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	
70	HCUCF89	484	Proliferation of preadipose cells (such as 3T3-L1 cells)	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp.,	Diabetes A highly preferred indication is diabetes. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g.,

due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below).	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired	wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin). Highly preferred	indications also include obesity, weight gain, and weight loss, as well as complications associated with obesity, weight gain, and weight loss. Preferred	embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating the above mentioned conditions, disorders,
Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present	which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells	isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth	M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.			
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					and diseases.
	HCI ICK 44	485	Protection from	Caspase Apoptosis Rescue.	A highly preferred
71			Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
1			Apoptosis.	rescue are well known in the art	includes a method for
			-	and may be used or routinely	stimulating endothelial cell
				modified to assess the ability of	growth. An alternative highly
				the polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method for
	-			and agonists or antagonists of	inhibiting endothelial cell
			-	the invention) to inhibit caspase	growth. A highly preferred
				protease-mediated apoptosis.	embodiment of the invention
				Exemplary assays for caspase	includes a method for
				apoptosis that may be used or	stimulating endothelial cell
				routinely modified to test	proliferation. An alternative
				caspase apoptosis rescue of	highly preferred embodiment of
				polypeptides of the invention	the invention includes a method
				(including antibodies and	for inhibiting endothelial cell
				agonists or antagonists of the	proliferation. A highly
				invention) include the assays	preferred embodiment of the
				disclosed in Romeo et al.,	invention includes a method for
				Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
-				(2000); Messmer et al., Br J	growth. An alternative highly
				Pharmacol 127(7): 1633-1640	preferred embodiment of the
				(1999); and J Atheroscler	invention includes a method for
				Thromb 3(2): 75-80 (1996); the	inhibiting endothelial cell
	_			contents of each of which are	growth. A highly preferred
				herein incorporated by reference	embodiment of the invention
				in its entirety. Endothelial cells	includes a method for
				that may be used according to	stimulating apoptosis of
				these assays are publicly	endothelial cells. An alternative
				available (e.g., through	highly preferred embodiment of
				commercial sources).	the invention includes a method
				Exemplary endothelial cells that	for inhibiting (e.g., decreasing)

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apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative	highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a	method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method	for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under	"Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic	stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease,	diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic
may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels	and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immine cell extravasation.					
						,

as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic	disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels	themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred	angiogenesis and/or cardiovascularization. Highly	preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications	include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and	retinal disorders. Highly preferred indications include neoplasms and cancer, such as,	(capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,	hemangioendothelioma, angiosarcoma, haemangiopericytoma,

lymhangioma	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver, and urinary cancer.	Preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Highly preferred	푾	disease, such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s disease	and Reynaud's phenomenom,	aneurysms, restenosis; venous	and lymphatic disorders such as	thrombophlebitis, lymphangitis,	and lymphedema; and other	vascular disorders such as	peripheral vascular disease, and	cancer. Highly preferred	indications also include trauma	such as wounds, burns, and	injured tissue (e.g., vascular	injury such as, injury resulting	from balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,
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ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke, graft	rejection, diabetic or other	retinopathies, thrombotic and	coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and vascular	disease. Preferred indications	include blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and immunodeficiencies	(e.g., as described below).
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Additional preferred indications include inflammation and	inflammatory disorders (such as	acute and chronic inflammatory	diseases, e.g., inflammatory	bowel disease and Crohn's	disease), and pain management.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	MCP-1 production. An	alternative highly preferred	embodiment of the invention	includes a method for inhibiting	(e.g., reducing) MCP-1	production. A highly	preferred indication is infection	(e.g., an infectious disease as	described below under	"Infectious Disease").	Additional highly preferred	indications include	_	disorders. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications
						MCP-1 FMAT. Assays for	immunomodulatory proteins	that are produced by a large	variety of cells and act to induce	chemotaxis and activation of	monocytes and T cells are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, induce	chemotaxis, and modulate	immune cell activation.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of cell	surface markers, such as	monocyte chemoattractant	protein (MCP), and the	activation of monocytes and T	cells. Such assays that may be	used or routinely modified to
						Production of MCP-		1																						
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test immunomodulatory and differentiation activity of polypeptides of the invention include assays disclosed in Mriaglia et al., 3 disclosed in Mriaglia et al., 4 munuofediciencies (e.g., as disclosed in Mriaglia et al., 4 munuofediciencies (e.g., as disclosed in Mriaglia et al., 4 munuofediciencies (e.g., as disclosed in Mriaglia et al., 4 munuofediciencies (e.g., as disclosed in Mriaglia et al., 4 munuofediciencies (e.g., as disclosed in Mriaglia et al., 4 munuofediciencies (e.g., as disclosed in Mriaglia et al., 4 munuofediciencies (e.g., as disclosed in Mriaglia et al., 4 monthocyotopenia, leukopenia, 18.2019.2955 gandulomatous activated by sorialsis, 18.2019.2955 gandulomatous activated by reference in its entirety. Human dendritic cells that may reactions to transplanted organs assays may be isolated using technique es since and fine and functional activities. Human dendritic cells are memigris foresterial and viral), and functional activities. Human dendritic cells are memigris foresterial and viral), and suspension culture, which, when a sorial and antigen presenting cells in a since indications as since and functional activities. Hypopropried archivical and propression of minute activities. Hypopropried activities. Hypopropried activities. Hypopropried activities. Hypopropried archivical and propression and cancers, such as leukemia, lymphoma, and functional activities active activities.																															\neg
	include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple scierosis and/or as	described below) allu	Immunodelliciencies (e.g., as	described below). I totalical	mancytonenia lenkonenia	thrombocytopenia, icanopenia,	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis (bacterial and viral),	Lyme Disease, asthma, and			(e.g., leukemia, lymphoma,	and/or as described below under	"Hyperproliferative Disorders").	Highly preferred indications	include neoplasms and cancers,	such as, leukemia, lymphoma,
	test immunomodulatory and diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Kowland et al.,	Lymphocytes: a practical	(2000): Satthaporn and Eremin,	J R Coll Surg Ednb 45(1):9-19	(2001); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which, when	activated by antigen and/or	cytokines, initiate and	upregulate T cell proliferation	and functional activities.			
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prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of GM-CSF. Highly preferred indications include indications include inflammatory disorders. An additional highly preferred indication is infection (e.g., as described below under "Infectious Disease". Highly preferred indications include blood disorders (e.g., in HIV infected patients), and/or as described below under "Immune Activity", "Blood-Related Disorders", and/or
	GM-CSF FMAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine. Assays for immunomodulatory proteins that promote the production of GM-CSF are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	CSF
	486
	72

"Cardiovascular Disorders").	Highly preferred indications	also include autoimmune	diseases (e.g., rheumatoid	arthritis, systemic lupus	erythematosis, multiple sclerosis	and/or as described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include asthma. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia (e.g., acute	lymphoblastic leukemia, and	acute myelogenous leukemia),	lymphoma (e.g., non-Hodgkin"s	lymphoma and Hodgkin"s	disease), and/or as described	below under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Highly preferred
(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	modulate the growth and	differentiation of leukocytes.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as GM-CSF,	and the activation of T cells.	Such assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Ye et al., J Leukoc	Biol (58(2):225-233, the	contents of each of which are	herein incorporated by reference	in its entirety. Natural killer	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC) or may be isolated using	techniques disclosed herein or
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otherwise known in the art. indications include: suppression of immune reactions to	hat	 	antibody-independent killing of and mobilizing nematopoletic	tumor cells and also recognize progenitor cells progenitor cells			 response. Preferred .	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutrophilia,	psoriasis, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease, and	allergy.		Negulation Caspass 1 to be cased a second and a second a secon	caspase apoptosis are well	apoptosis in caspase apoptosis are well pancreatic beta cells. known in the art and may be	apoptosis in caspase apoptosis are well pancreatic beta cells. known in the art and may be used or routinely modified to
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				_																				7.2	72	72

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asse be d d d d d d d d d d d d d d d d d d		agonists or antagonists of the	(e.g., renai lailuie, iichiiichauiy
and is is a different state of the passe of		invention) to promote caspase	and/or other diseases and
al., P.		protease-mediated apoptosis.	disorders as described in the
		Apoptosis in pancreatic beta is	"Renal Disorders" section
		associated with induction and	below), diabetic neuropathy,
		progression of diabetes.	nerve disease and nerve damage
::		Exemplary assays for caspase	(e.g., due to diabetic
Ф :: E Д О Г Т О Т Г Т О О Т О О Т Т Т Т Т Т Т Т		apoptosis that may be used or	neuropathy), blood vessel
tion rithe ays retal., the can retail. The can retail. The can retail rith. The can retail ri		routinely modified to test capase	blockage, heart disease, stroke,
ition 17 17 18 19 19 19 19 19 19 19		apoptosis activity of	impotence (e.g., due to diabetic
ays rads, et al., h h c c c c c c c c c c c c c c c c c		polypeptides of the invention	neuropathy or blood vessel
ays r, et al., et al., et al., c.		(including antibodies and	blockage), seizures, mental
al., H H H H H H H H H H H H H H H H H H H		agonists or antagonists of the	confusion, drowsiness,
		invention) include the assays	nonketotic hyperglycemic-
:.		disclosed in: Loweth, AC, et al.,	hyperosmolar coma,
7		FEBS Lett, 400(3):285-8	cardiovascular disease (e.g.,
J J 4-7 60 (2001); r ett, hang, r hang, r L22- Vasc		(1997); Saini, KS, et al.,	heart disease, atherosclerosis,
br J 94 11., 14.7 9 (2001); Lett, Zhang, 1): 122- 1) Vasc 1) Vasc 1000); and		Biochem Mol Biol Int,	microvascular disease,
001); 19 19, 19, 19, 10, 10, 10, 10, 10, 10, 10, 10, 10, 10		39(6):1229-36 (1996);	hypertension, stroke, and other
001); 19, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18		Krautheim, A., et al., Br J	diseases and disorders as
001); 19 18, 11 18, 12 2- 2- 2- and and		Pharmacol, 129(4):687-94	described in the "Cardiovascular
001); '' '' '' '' '' '' '' '' '' '' '' '' ''		(2000); Chandra J, et al.,	Disorders" section below),
18, 18, 18, 18, 18, 18, 18, 18, 18, 18,		Diabetes, 50 Suppl 1:S44-7	dyslipidemia, endocrine
-9 (2001); Lett, Lett, Zhang, Ele et S): 122- J Vasc 0000; and		(2001); Suk K, et al., J	disorders (as described in the
S Lett,); Zhang,); Lee et -3): 122- 1, J Vasc 2000); and		Immunol, 166(7):4481-9 (2001);	
); Zhang, ; ; Lee et ; ; Le et ; ; Lo et ; ; 122- ; ; J Vasc ; ; , 32000); and ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ;		Tejedo J, et al., FEBS Lett,	
); Lee et -3): 122- ., J Vasc 2000); and		459(2):238-43 (1999); Zhang,	impairment (e.g., diabetic
); Lee et -3): 122- 1., J Vasc 2000); and		S., et al., FEBS Lett,	retinopathy and blindness),
		455(3):315-20 (1999); Lee et	ulcers and impaired wound
		al., FEBS Lett 485(2-3): 122-	healing, and infection (e.g.,
		126 (2000); Nor et al., J Vasc	infectious diseases and disorders
	_	Res 37(3); 209-218 (2000); and	as described in the "Infectious

Atheroscler Thromb 3(2): 75-8 (1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RNh-m. RNh-ris a rat adherent pancreatic better is a rat adherent produce and secrete islet polypeptide hormones, and produce insulin somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1980 77:3519. HCWAE64 487 Regulation of Assays for the regulation of transcription via transcription via transcription via transcription through the DMEF1 response element are element in wall-known in the art and may					Karsan and Harlan, J	Diseases" section below,	
Regulation of transcription via DMEF1 response element in					Atheroscler Thromb 3(2): 75-80	especially of the urinary tract	
487 Regulation of transcription via DMEF1 response element in				•	(1996); the contents of each of	and skin), carpal tunnel	
487 Regulation of transcription via DMEF1 response element in					which are herein incorporated	syndrome and Dupuytren's	
487 Regulation of transcription via DMEF1 response element in					by reference in its entirety.	contracture). An additional	
487 Regulation of transcription via DMEF1 response element in					Pancreatic cells that may be	highly preferred indication is	
487 Regulation of transcription via DMEF1 response element in				•	used according to these assays	obesity and/or complications	
487 Regulation of transcription via DMEF1 response element in					are publicly available (e.g.,	associated with obesity.	
487 Regulation of transcription via DMEF1 response element in					through the ATCC) and/or may	Additional highly preferred	
487 Regulation of transcription via DMEF1 response element in					be routinely generated.	indications include weight loss	
487 Regulation of transcription via DMEF1 response element in					Exemplary pancreatic cells that	or alternatively, weight gain.	
487 Regulation of transcription via DMEF1 response element in					may be used according to these	Aditional highly preferred	
487 Regulation of transcription via DMEF1 response element in					assays include RIN-m. RIN-m	indications are complications	
487 Regulation of transcription via DMEF1 response element in					is a rat adherent pancreatic beta	associated with insulin	
487 Regulation of transcription via DMEF1 response element in					cell insulinoma cell line derived	resistance.	
487 Regulation of transcription via DMEF1 response element in					from a radiation induced		
487 Regulation of transcription via DMEF1 response element in					transplantable rat islet cell		
487 Regulation of transcription via DMEF1 response element in					tumor. The cells produce and		
487 Regulation of transcription via DMEF1 response element in					secrete islet polypeptide		
487 Regulation of transcription via DMEF1 response element in					hormones, and produce insulin,		
487 Regulation of transcription via DMEF1 response element in	_				somatostatin, and possibly		
487 Regulation of transcription via DMEF1 response element in					glucagon. ATTC: #CRL-2057		
487 Regulation of transcription via DMEF1 response element in					Chick et al. Proc. Natl. Acad.		
487 Regulation of transcription via DMEF1 response element in					Sci. 1977 74:628; AF et al.		
Regulation of transcription via DMEF1 response element in					Proc. Natl. Acad. Sci. 1980		
487 Regulation of transcription via DMEF1 response element in					77:3519.		
transcription via DMEF1 response element in		ICWAE64	487	Regulation of	Assays for the regulation of	A highly preferred indication is	
e e				transcription via	transcription through the	diabetes mellitus. Additional	
				DMEF1 response	DMEF1 response element are	highly preferred indications	
			-	element in	well-known in the art and may	include complications	
adipocytes and pre- be used or routinely modifie				adipocytes and pre-	be used or routinely modified to	associated with diabetes (e.g.,	
adinocytes assess the ability of	•			adinocytes	assess the ability of	diabetic retinopathy, diabetic	

				"Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J	Diseases" section below, especially of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly
				4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference	preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
				in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	
73	HCWAE64	487	Activation of transcription through	Assays for the activation of transcription through the cAMP	A highly preferred indication is obesity and/or complications

				Malm, Methods in Enzymol	dyslipidemia, endocrine
				et al., Proc Natl Acad Sci USA	"Endocrine Disorders" section
				85:6342-6346 (1988); Reusch et	below), neuropathy, vision
				al., Mol Cell Biol 20(3):1008-	impairment (e.g., diabetic
				1020 (2000); and Klemm et al.,	retinopathy and blindness),
				J Biol Chem 273:917-923	ulcers and impaired wound
				(1998), the contents of each of	healing, and infection (e.g.,
				which are herein incorporated	infectious diseases and disorders
-				by reference in its entirety. Pre-	as described in the "Infectious
		,		adipocytes that may be used	Diseases" section below,
				according to these assays are	especially of the urinary tract
				publicly available (e.g., through	and skin), carpal tunnel
				the ATCC) and/or may be	syndrome and Dupuytren's
				routinely generated. Exemplary	contracture). Additional highly
				mouse adipocyte cells that may	preferred indications are
				be used according to these	complications associated with
				assays include 3T3-L1 cells.	insulin resistance.
				3T3-L1 is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
			-	fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
	HCWAE64	487	Activation of	Assays for the activation of	A highly preferred indication is obesity and/or complications
c/			transcription through	Response Flement (SRE) are	associated with obesity.
			olomont in ano	well brown in the ort and may	Additional highly preferred
			edinont III pre-	be used or routinely modified to	indications include weight loss
			auipocytes.	חר מספר טו ורשוווים איויים ווייים ווייים	וומוסווס וויסווס וויסווסווס וויסווסווסווסווסווסווסווסווסווסווסווסווס

assess the ability of	or alternatively, weight game.
polypeptides of the invention	An additional highly preferred
(including antibodies and	indication is diabetes mellitus.
agonists or antagonists of the	An additional highly preferred
invention) to regulate the serum	indication is a complication
response factors and modulate	associated with diabetes (e.g.,
the expression of genes involved	diabetic retinopathy, diabetic
in growth. Exemplary assays	nephropathy, kidney disease
for transcription through the	(e.g., renal failure, nephropathy
SRE that may be used or	and/or other diseases and
routinely modified to test SRE	disorders as described in the
activity of the polypeptides of	"Renal Disorders" section
the invention (including	below), diabetic neuropathy,
antibodies and agonists or	nerve disease and nerve damage
antagonists of the invention)	(e.g., due to diabetic
include assays disclosed in	neuropathy), blood vessel
Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
(1998); Cullen and Malm,	impotence (e.g., due to diabetic
Methods in Enzymol 216:362-	neuropathy or blood vessel
368 (1992); Henthorn et al.,	blockage), seizures, mental
Proc Natl Acad Sci USA	confusion, drowsiness,
85:6342-6346 (1988); and Black	nonketotic hyperglycemic-
et al., Virus Genes 12(2):105-	hyperosmolar coma,
117 (1997), the content of each	cardiovascular disease (e.g.,
of which are herein incorporated	heart disease, atherosclerosis,
by reference in its entirety. Pre-	microvascular disease,
adipocytes that may be used	hypertension, stroke, and other
according to these assays are	diseases and disorders as
publicly available (e.g., through	described in the "Cardiovascular
the ATCC) and/or may be	Disorders" section below),
routinely generated. Exemplary	dyslipidemia, endocrine
mouse adipocyte cells that may	disorders (as described in the
be used according to these	"Endocrine Disorders" section
1	the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these

below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below). Additional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies
assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
	487
	HCWAE64
	73

response development.	(e.g., as described below).
Exemplary assays for	Preferred indications include
transcription through the	neoplastic diseases (e.g.,
 GATA3 response element that	leukemia, lymphoma,
may be used or routinely	melanoma, prostate, breast,
modified to test GATA3-	lung, colon, pancreatic,
response element activity of	esophageal, stomach, brain,
polypeptides of the invention	liver, and urinary tract cancers
(including antibodies and	and/or as described below under
agonists or antagonists of the	"Hyperproliferative Disorders").
invention) include assays	Other preferred indications
disclosed in Berger et al., Gene	include benign dysproliferative
66:1-10 (1998); Cullen and	disorders and pre-neoplastic
Malm, Methods in Enzymol	conditions, such as, for example,
216:362-368 (1992); Henthorn	hyperplasia, metaplasia, and/or
et al., Proc Natl Acad Sci USA	dysplasia. Preferred indications
85:6342-6346 (1988); Flavell et	include anemia, pancytopenia,
al., Cold Spring Harb Symp	leukopenia, thrombocytopenia,
Quant Biol 64:563-571 (1999);	leukemias, Hodgkin's disease,
 Rodriguez-Palmero et al., Eur J	acute lymphocytic anemia
Immunol 29(12):3914-3924	(ALL), plasmacytomas, multiple
(1999); Zheng and Flavell, Cell	myeloma, Burkitt's lymphoma,
89(4):587-596 (1997); and	arthritis, AIDS, granulomatous
Henderson et al., Mol Cell Biol	disease, inflammatory bowel
14(6):4286-4294 (1994), the	disease, sepsis, neutropenia,
contents of each of which are	neutrophilia, psoriasis,
herein incorporated by reference	suppression of immune
in its entirety. Mast cells that	reactions to transplanted organs
may be used according to these	and tissues, hemophilia,
 assays are publicly available	hypercoagulation, diabetes
 (e.g., through the ATCC).	mellitus, endocarditis,
Exemplary human mast cells	meningitis, and Lyme Disease.
that may be used according to	

				these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	
73	HCWAE64	487	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below).
				transcription through the NFAT response element that may be	neoplastic diseases (e.g., leukemia, lymphoma,

_	used or routinely modified to	melanoma prostate breast.
	test NFAT-response element	lung, colon, pancreatic,
	activity of polypeptides of the	esophageal, stomach, brain,
	invention (including antibodies	liver, and urinary tract cancers
	and agonists or antagonists of	and/or as described below under
	the invention) include assays	"Hyperproliferative Disorders").
	disclosed in Berger et al., Gene	Other preferred indications
	66:1-10 (1998); Cullen and	include benign dysproliferative
	Malm, Methods in Enzymol	disorders and pre-neoplastic
	216:362-368 (1992); Henthorn	conditions, such as, for example,
	et al., Proc Natl Acad Sci USA	hyperplasia, metaplasia, and/or
	85:6342-6346 (1988); De Boer	dysplasia. Preferred indications
	et al., Int J Biochem Cell Biol	include anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali et	leukopenia, thrombocytopenia,
	al., J Immunol 165(12):7215-	leukemias, Hodgkin's disease,
	 7223 (2000); Hutchinson and	acute lymphocytic anemia
	McCloskey, J Biol Chem	(ALL), plasmacytomas, multiple
	270(27):16333-16338 (1995),	myeloma, Burkitt's lymphoma,
	and Turner et al., J Exp Med	arthritis, AIDS, granulomatous
	188:527-537 (1998), the	disease, inflammatory bowel
	contents of each of which are	disease, sepsis, neutropenia,
	 herein incorporated by reference	neutrophilia, psoriasis,
	in its entirety. Mast cells that	suppression of immune
	may be used according to these	reactions to transplanted organs
	assays are publicly available	and tissues, hemophilia,
	(e.g., through the ATCC).	hypercoagulation, diabetes
	 Exemplary human mast cells	mellitus, endocarditis,
	that may be used according to	meningitis, and Lyme Disease.
	these assays include the HMC-1	
	cell line, which is an immature	
	 human mast cell line established	
	from the peripheral blood of a	
	patient with mast cell leukemia,	

				and exhibits many characteristics of immature mast cells.	
73	HCWAE64	487	Activation of transcription through	Assays for the activation of transcription through the	Highly preferred indications include blood disorders (e.g., as
3			NFAT response	Nuclear Factor of Activated T	described below under "Immune
			element in immune	cells (NFAT) response element	Activity", "Blood-Related
			cells (such as natural	are well-known in the art and	Disorders", and/or
			killer cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability of	Highly preferred indications
				polypeptides of the invention	include autoimmune diseases
				(including antibodies and	(e.g., rheumatoid arthritis,
				agonists or antagonists of the	systemic lupus erythematosis,
				invention) to regulate NFAT	multiple sclerosis and/or as
				transcription factors and	described below),
		1, 27		modulate expression of genes	immunodeficiencies (e.g., as
				involved in immunomodulatory	described below), boosting a T
				functions. Exemplary assays for	cell-mediated immune response,
				transcription through the NFAT	and suppressing a T cell-
				response element that may be	mediated immune response.
				used or routinely modified to	Additional highly preferred
				test NFAT-response element	indications include
				activity of polypeptides of the	inflammation and inflammatory
				invention (including antibodies	disorders. An additional highly
	-			and agonists or antagonists of	preferred indication is infection
				the invention) include assays	(e.g., an infectious disease as
				disclosed in Berger et al., Gene	described below under
		·-		66:1-10 (1998); Cullen and	"Infectious Disease").
				Malm, Methods in Enzymol	Preferred indications include
				216:362-368 (1992); Henthorn	neoplastic diseases (e.g.,
				et al., Proc Natl Acad Sci USA	leukemia, lymphoma, and/or as
			ī.	85:6342-6346 (1988);	described below under

	Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer	"Hyperproliferative Disorders"). Preferred indications include
	et al., Int J Biochem Cell Biol	neoplasms and cancers, such as,
	31(10):1221-1236 (1999);	for example, leukemia,
	Fraser et al., Eur J Immunol	lymphoma, and prostate, breast,
	29(3):838-844 (1999); and	lung, colon, pancreatic,
	Yeseen et al., J Biol Chem	esophageal, stomach, brain,
	268(19):14285-14293 (1993),	liver and urinary cancer. Other
	the contents of each of which	preferred indications include
	are herein incorporated by	benign dysproliferative
	reference in its entirety. NK	disorders and pre-neoplastic
	cells that may be used according	conditions, such as, for example,
	to these assays are publicly	hyperplasia, metaplasia, and/or
	available (e.g., through the	dysplasia. Preferred
	ATCC). Exemplary human NK	indications also include anemia,
	cells that may be used according	pancytopenia, leukopenia,
	to these assays include the NK-	thrombocytopenia, Hodgkin's
	YT cell line, which is a human	disease, acute lymphocytic
	natural killer cell line with	anemia (ALL), plasmacytomas,
	cytolytic and cytotoxic activity.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted organs
		and tissues, hemophilia,
		hypercoagulation, diabetes
,		mellitus, endocarditis,
		meningitis, Lyme Disease,
		asthma and allergy.

		TO HOUSE	Assays for the activation of	A preferred embodiment of
		transcription through	transcription through the Serum	the invention includes a method
		serum response	Response Element (SRE) are	for inhibiting (e.g., reducing)
		element in immune	well-known in the art and may	TNF alpha production. An
		cells (such as natural	be used or routinely modified to	alternative highly preferred
		killer cells).	assess the ability of	embodiment of the invention
			polypeptides of the invention	includes a method for
			(including antibodies and	stimulating (e.g., increasing)
			agonists or antagonists of the	TNF alpha production.
			invention) to regulate serum	Preferred indications include
			response factors and modulate	blood disorders (e.g., as
			the expression of genes involved	described below under "Immune
			in growth and upregulate the	Activity", "Blood-Related
			function of growth-related genes	Disorders", and/or
-			in many cell types. Exemplary	"Cardiovascular Disorders"),
			assays for transcription through	Highly preferred indications
			the SRE that may be used or	include autoimmune diseases
			routinely modified to test SRE	(e.g., rheumatoid arthritis,
			activity of the polypeptides of	systemic lupus erythematosis,
			the invention (including	Crohn"s disease, multiple
			antibodies and agonists or	sclerosis and/or as described
			antagonists of the invention)	below), immunodeficiencies
			include assays disclosed in	(e.g., as described below),
			Berger et al., Gene 66:1-10	boosting a T cell-mediated
			(1998); Cullen and Malm,	immune response, and
			Methods in Enzymol 216:362-	suppressing a T cell-mediated
			368 (1992); Henthorn et al.,	immune response. Additional
			Proc Natl Acad Sci USA	highly preferred indications
	-		85:6342-6346 (1988); Benson et	include inflammation and
			al., J Immunol 153(9):3862-	inflammatory disorders, and
			3873 (1994); and Black et al.,	treating joint damage in patients
			Virus Genes 12(2):105-117	with rheumatoid arthritis. An
			(1997), the content of each of	additional highly preferred

																													_			
indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophilia,	psoriasis, suppression of
which are herein incorporated	by reference in its entirety.	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary T cells that	may be used according to these	assays include the NK-YT cell	line, which is a human natural	killer cell line with cytolytic and	cytotoxic activity.								-			**************************************		•									
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antibodies and agonists or dysplasia. Preferred indications antagonists of the invention) include autoimmune diseases include assays disclosed in 6cg., rheumatoid arthritis, Berger et al., Gene 6ci.1-0 multiple sclerosis and/or as Methods in Enzymol 216:362–368 (1988); Methods in Enzymol 216:362–346 (1988); Matikainen et al., Blood Matikainen et al., Blood Matikainen et al., J Immunol 155(10):4582–4587 (1999); and mediated immune response. Hentitinen et al., J Immunol 155(10):4582–4587 (1999); and mediated immune response. Hentitinen et al., J Immunol 155(10):4582–4587 (1995), the inflammation and contents of each of which are inflammation and suppressing a T cell-636():1980-1991 (1999); and autoin the contents of each of which are inflammatory disorders. Highly herein incorporated by reference preferred indications include in its entirely. Exemplary bood disorders (e.g., as human T cells, such as the described below under "Immune SUPT cell line, that may be used according to these assays are Disorders", and/or an infection granulomatosus disease and malignant osteoporosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, infectional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, panoytopenia,	2- 2- in the contract of the c
antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362- 368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Mallm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Marikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).

acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.		A highly preferred indication includes allergy. A highly preferred indication includes arthma. A highly preferred indication includes rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related
		Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of genes important for Th2 immune response development. Exemplary assays for transcription through the
·	CD71 in Human T cells	Activation of transcription through GATA-3 response element in immune cells (such as T-cells).
	488	489
	HCWFU39	HCWUL09
	74	75

	GATA3 response element that	Disorders", and/or
	may be used or routinely	"Cardiovascular Disorders").
	modified to test GATA3-	Preferred indications include
	response element activity of	autoimmune diseases (e.g.,
	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) include assays	below) and immunodeficiencies
	disclosed in Berger et al., Gene	(e.g., as described below).
	66:1-10 (1998); Cullen and	Preferred indications include
	Malm, Methods in Enzymol	neoplastic diseases (e.g.,
	 216:362-368 (1992); Henthorn	leukemia, lymphoma,
	et al., Proc Natl Acad Sci USA	melanoma, and/or as described
	85:6342-6346 (1988); Flavell et	below under "Hyperproliferative
	al., Cold Spring Harb Symp	Disorders"). Preferred
	Quant Biol 64:563-571 (1999);	indications include neoplasms
	Rodriguez-Palmero et al., Eur J	and cancer, such as, for
	Immunol 29(12):3914-3924	example, leukemia, lymphoma,
	(1999); Zheng and Flavell, Cell	melanoma, and prostate, breast,
	89(4):587-596 (1997); and	lung, colon, pancreatic,
	Henderson et al., Mol Cell Biol	esophageal, stomach, brain,
	14(6):4286-4294 (1994), the	liver and urinary cancer. Other
	contents of each of which are	preferred indications include
	herein incorporated by reference	benign dysproliferative
	 in its entirety. T cells that may	disorders and pre-neoplastic
	be used according to these	conditions, such as, for example,
	assays are publicly available	hyperplasia, metaplasia, and/or
	(e.g., through the ATCC).	dysplasia. Preferred
	 Exemplary mouse T cells that	indications include anemia,
	may be used according to these	pancytopenia, leukopenia,
	assays include the HT2 cell line,	thrombocytopenia, leukemias,
	which is a suspension culture of	Hodgkin's disease, acute
	IL-2 dependent T cells that also	lymphocytic anemia (ALL),

HDHAA42	490	Production of IFNgamma using Natural Killer cells	respond to IL-4. IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine.	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. A highly preferred embodiment of the invention includes a method for	
			iFNg promotes TH1 and inhibits TH2; promotes lgG2a and inhibits IgE; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders", "Gardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with	

e g		er		•				_	.i.				e,		50	-							<u>~</u>	_						_	ive	_
natosus disea	steoporosis,	ned below unc	ase"). Highly	ions include	ease (e.g.,	ritis, systemic	osis, multiple	as described	deficiency (e.	ow), boosting	immune	ppressing a T	ımune respon	ly-dependent	es, suppressir	lent immune	ing innate	nmune	uppressing	and immune	itional highly	tions include	d inflammato	ional preferre	ide idiopathic	sis. Highly	tions include	ses (e.g.,	noma,	or as describe	yperproliferat	1. 1
chronic granulomatosus disease	and malignant osteoporosis,	and/or as described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency (e.g.,	as described below), boosting a	T cell-mediated immune	response, and suppressing a T	cell-mediated immune response,	boosting antibody-dependent	immune responses, suppressing	antibody-dependent immune	responses, boosting innate	immunity and immune	responses, and suppressing	innate immunity and immune	responses. Additional highly	preferred indications include	inflammation and inflammatory	disorders. Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative	Disardars" Uiahly proferred
				mediate			<u> </u>							Ţ				de the assays		creening 4:193-		a practical	ter 6:138-160					Annu Rev Immunol 15:749-795				- In the second second
invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for immunomodulatory	proteins evaluate the production	of cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad Sci	856:22-32 (1998	Annu Rev Imm	(1997), and Rheumatology	(Oxford) 38(3):214-20 (1999),	the contents of each of which	are herein incorporated by
																													-			

					reference in its entirety Natural	indications include neoplasms
used according to these assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocyses that have cytotoxic activity but do bind antigen. NK cells show antibodyindependent killing of tumor cells and also recognize antibody bound on target cells, via NK Fe receptors, leading to cell-mediated cytotoxicity.					Killer (NK) cells that may be	and cancers, such as, for
are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells how antibodyindependent killing of tumor cells and also recognize antibody bound on target cells, via NK Fe receptors, leading to cell-mediated cytotoxicity.		-			used according to these assays	example, leukemia, lymphoma,
through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.					are publicly available (e.g.,	melanoma, and prostate, breast,
isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody- independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.				•	through the ATCC) or may be	lung, colon, pancreatic,
disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.					isolated using techniques	esophageal, stomach, brain,
known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody- independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.					disclosed herein or otherwise	liver and urinary cancer. Other
(NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.					known in the art. Natural killer	preferred indications include
lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody- independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.					(NK) cells are large granular	benign dysproliferative
activity but do bind antigen. NK cells show antibody- independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.			-		lymphocytes that have cytotoxic	disorders and pre-neoplastic
NK cells show antibody- independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.	•	-			activity but do bind antigen.	conditions, such as, for example,
independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.					NK cells show antibody-	hyperplasia, metaplasia, and/or
cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity. cell-mediated cytotoxicity. i			-		independent killing of tumor	dysplasia. Preferred
antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity. cell-mediated cytotoxicity.		-			cells and also recognize	indications include anemia,
via NK Fc receptors, leading to cell-mediated cytotoxicity. cell-mediated cytotoxicity.					antibody bound on target cells,	pancytopenia, leukopenia,
cell-mediated cytotoxicity.					via NK Fc receptors, leading to	thrombocytopenia, Hodgkin's
y Production of IL-6 FMAT. IL-6 is produced					cell-mediated cytotoxicity.	disease, acute lymphocytic
, , , , , , , , , , , , , , , , , , ,					•	anemia (ALL), plasmacytomas,
, , , , , , , , , , , , , , , , , , ,			. 1			multiple myeloma, Burkitt's
, , , , , , , , , , , , , , , , , , ,	-					lymphoma, arthritis, AIDS,
, , , , , , , , , , , , , , , , , , ,		-				granulomatous disease,
, , , , , , , , , , , , , , , , , , ,						inflammatory bowel disease,
, , , , , , , , , , , , , , , , , , ,	-					sepsis, neutropenia,
, , , , , , , , , , , , , , , , , , ,						neutrophilia, psoriasis,
, Yell Production of IL-6 FMAT. IL-6 is produced						suppression of immune
, , , , , , , , , , , , , , , , , , ,	-					reactions to transplanted organs
y Production of IL-6 FMAT. IL-6 is produced						and tissues, hemophilia,
7 Production of IL-6 FMAT. IL-6 is produced						hypercoagulation, diabetes
491 Production of IL-6 FMAT. IL-6 is produced						mellitus, endocarditis,
491 Production of IL-6 FMAT. IL-6 is produced						meningitis, Lyme Disease,
491 Production of IL-6 IL-6 FMAT. IL-6 is produced						asthma and allergy.
		DHFR76	491	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred embodiment

of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid	arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include inflammation and
by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of

T cell proliferation and	inflammatory
functional activities. Such	disorders.Additional highly
assays that may be used or	preferred indications include
routinely modified to test	asthma and allergy. Highly
immunomodulatory and	preferred indications include
diffferentiation activity of	neoplastic diseases (e.g.,
polypeptides of the invention	myeloma, plasmacytoma,
(including antibodies and	leukemia, lymphoma,
agonists or antagonists of the	melanoma, and/or as described
invention) include assays	below under "Hyperproliferative
disclosed in Miraglia et al., J	Disorders"). Highly preferred
Biomolecular Screening 4:193-	indications include neoplasms
204(1999); Rowland et al.,	and cancers, such as, myeloma,
"Lymphocytes: a practical	plasmacytoma, leukemia,
approach" Chapter 6:138-160	lymphoma, melanoma, and
(2000); and Verhasselt et al., J	prostate, breast, lung, colon,
Immunol 158:2919-2925	pancreatic, esophageal, stomach,
(1997), the contents of each of	brain, liver and urinary cancer.
which are herein incorporated	Other preferred indications
by reference in its entirety.	include benign dysproliferative
Human dendritic cells that may	disorders and pre-neoplastic
be used according to these	conditions, such as, for example,
assays may be isolated using	hyperplasia, metaplasia, and/or
techniques disclosed herein or	dysplasia. Preferred indications
otherwise known in the art.	include anemia, pancytopenia,
Human dendritic cells are	leukopenia, thrombocytopenia,
antigen presenting cells in	Hodgkin's disease, acute
suspension culture, which, when	lymphocytic anemia (ALL),
activated by antigen and/or	multiple myeloma, Burkitt's
cytokines, initiate and	lymphoma, arthritis, AIDS,
upregulate T cell proliferation	granulomatous disease,
and functional activities.	inflammatory bowel disease,
	sepsis, neutropenia,

82	HDPCW16	492	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, mellitus, endocarditis, mellitus, and Lyme Disease. An additonal preferred indication is infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as as described below under "Immune Activity" "Blood-Related
				evaluate the production of chemokines, such as macrophage inflammatory	Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications

nrotein 1 alnha (MIP-1a) and	include autoimmune diseases
the activation of	(e.g., rheumatoid arthritis,
monocytes/macrophages and T	systemic lupus erythematosis,
cells. Such assays that may be	multiple sclerosis and/or as
used or routinely modified to	described below) and
test immunomodulatory and	immunodeficiencies (e.g., as
chemotaxis activity of	described below). Additional
polypeptides of the invention	highly preferred indications
(including antibodies and	include inflammation and
agonists or antagonists of the	inflammatory disorders.
invention) include assays	Preferred indications also
disclosed in Miraglia et al., J	include anemia, pancytopenia,
Biomolecular Screening 4:193-	leukopenia, thrombocytopenia,
204(1999); Rowland et al.,	Hodgkin's disease, acute
"Lymphocytes: a practical	lymphocytic anemia (ALL),
approach" Chapter 6:138-160	plasmacytomas, multiple
(2000); Satthaporn and Eremin,	myeloma, Burkitt's lymphoma,
J R Coll Surg Ednb 45(1):9-19	arthritis, AIDS, granulomatous
(2001); Drakes et al., Transp	disease, inflammatory bowel
Immunol 8(1):17-29 (2000);	disease, sepsis, neutropenia,
Verhasselt et al., J Immunol	neutrophilia, psoriasis,
158:2919-2925 (1997); and	suppression of immune
Nardelli et al., J Leukoc Biol	reactions to transplanted organs
65:822-828 (1999), the contents	and tissues, hemophilia,
of each of which are herein	hypercoagulation, diabetes
incorporated by reference in its	mellitus, endocarditis,
entirety. Human dendritic cells	meningitis, Lyme Disease,
that may be used according to	asthma, and allergy.
these assays may be isolated	Preferred indications also
using techniques disclosed	include neoplastic diseases (e.g.,
herein or otherwise known in	leukemia, lymphoma, and/or as
the art. Human dendritic cells	described below under
are antigen presenting cells in	"Hyperproliferative Disorders").

				that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	
79	HDPD172	493	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention).	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production.
				response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or	blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases
				routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10	(e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated

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pu	l-mediat	Additio	lications	on and	ders, anc	ge in pat	hritis. A	eferred	High	s includ	(e.g.,	ia, and/o	der	: Disorde	y preferr	neoplasi	s, for	lympho	(e.g.,	solid	e, breast	atic,	h, brain	incer. Ot	s includ	ıtive	eoplastic	, for exa	lasia, and	red	anemia,	openia.
sponse, a	g a T cell	sponse.	erred inc	lammatic	ry disor	nt damag	natoid ard	nighly pr	is sepsis.	ndication	diseases	ymphon	elow un	liferative	ly, highly	include	s, such a	eukemia,	glioma	glioma),	d prostat	i, pancre	l, stomac	rinary ca	ndication	prolifera	nd pre-n	such as	a, metap	Prefer	include	nia, leuk
immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,
ii.			-iu		<u> </u>								g							=	<u>,</u>		es	<u>=</u>	ď	<u>Ā</u>	Ġ.	<u> </u>	<u> </u>	<u>.</u>	프	<u>~</u>
alm,	216:362	et al.,	SA	Bensor	:3862-	ck et al.,	5-117	each of	rporated	irety. T	l accord	blicly	th the	F cells th	g to the	Z-YT ce	n natura	tolytic a														
(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson et	al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary T cells that	may be used according to these	assays include the NK-YT cell	line, which is a human natural	killer cell line with cytolytic and	vity.													
); Culler	ods in El	1992); H	Natl Aca	42-6346	[mmnno	(1994);	Genes 1), the co	are her	erence i	hat may	se assay	ıble (e.g	C). Exel	e nsed	s includ	which is	cell line	cytotoxic activity.													
(1998	Metho	368 (1	Proc]	85:63	al., J]	3873	Virus	(1997	which	by ref	cells t	to the	availa	ATC	may b	assay	line, 1	killer	cytoto	•												
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thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia,	psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An	infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune	Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as
		Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be
		Production of IL-10 and activation of T- cells.	
		493	
		HDPDI72	
		79	

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described below),	described below), boosting a T	cell-mediated immune response,	and suppressing a T cell-	mediated immune response.																											
used or routinely modified to	polypeptides and antibodies of	the invention (including agonists	or antagonists of the invention)	to modulate IL-10 production	and/or T-cell proliferation	include, for example, assays	such as disclosed and/or cited	in: Robinson, DS, et al., "Th-2	cytokines in allergic disease" Br	Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the contents	of each of which are herein	incorporated by reference in	their entirety. Exemplary cells	that may be used according to	these assays include Th2 cells.	IL10 secreted from Th2 cells	may be measured as a marker of	Th2 cell activation. Th2 cells	are a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation of	Th2 cells play a major role in	the initiation and pathogenesis	of allergy and asthma. Primary	Thelper 2 cells are generated
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of the same of the					via in vitro culture under Th2	
HDPDJ58 494 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention proliferation. Semplary assays for ERK kinase activity that may be used or routinely modified to to est ERK kinase-induced activity of polypeptides of the invention in the invention including antibodies and agonists or antagonists of the invention including antibodies and agonists or antagonists of the invention (including antagonists of the invention) include the assays disclosed in Forter et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochen Soc						
HDPDJ58 494 Activation of Kinase assay. Kinase assays, Adipocyte ERK for example an Elk-1 kinase Signaling Pathway growth of transduction that regulate cell proliferation of are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention in (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation. Exemplary assays for ERK kinase-induced activity of polypeptides of the invention induced					polarizing conditions using	
Adipocyte ERK for example an EIk-1 kinase Signaling Pathway assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase-induced activity of polypeptides of the invention include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes (1072):126-132 (1999); Kyriakis JM, Biochem Soc					isolated from cord blood.	
Adipocyte ERK Signaling Pathway Signaling Pathway Signaling Pathway Signaling Pathway Transduction that regulate cell proliferation or differentiation may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase- induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8- 9):1101-1110 (1998), Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc		HDPDIS8	494	Activation of	Kinase assay. Kinase assays.	A highly preferred
Signaling Pathway ransduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase- induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8- 9);1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes (1070);126-132 (1999); Kyriakis JM, Biochem Soc	0	00001011	1	Adinocyte FRK	for example an Elk-1 kinase	embodiment of the invention
transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc	00			Signaling Pathway	assav. for ERK signal	includes a method for
ation and thility of the lility of the linhibit sion, and con and linhibit stivity the leptides or lion) sed in p Clin oc				(ma., aa.)	transduction that regulate cell	stimulating adipocyte
and lility of the lility of the linhibit sion, and con linhibit sion, and con linhibit sion) seed in p Clin p Clin oc					proliferation or differentiation	proliferation. An alternative
ility of the tinnibit sinhibit					are well known in the art and	highly preferred embodiment of
tility of the tinnibit sinhibit sinhibit sinhibit sinhibit strivity nely assere of the section oc					may be used or routinely	the invention includes a method
y y the series of the series o					modified to assess the ability of	for inhibiting adipocyte
y trees and control of the second of the sec					polypeptides of the invention	proliferation. A highly
y y t t y t t s s s s s s s s s s s s s					(including antibodies and	preferred embodiment of the
y ty					agonists or antagonists of the	invention includes a method for
vity ty ty ty ly e- e- ridges ridges the din 9(8-					invention) to promote or inhibit	stimulating adipocyte
vity 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1					cell proliferation, activation, and	differentiation. An alternative
vity ly					differentiation. Exemplary	highly preferred embodiment of
des des lin lin lin					assays for ERK kinase activity	the invention includes a method
des in (8-					that may be used or routinely	for inhibiting adipocyte
des in (8-			-		modified to test ERK kinase-	differentiation. A highly
ii & ii					induced activity of polypeptides	preferred embodiment of the
ii % iil					of the invention (including	invention includes a method for
ii -8) iil					antibodies and agonists or	stimulating (e.g., increasing)
ii (8-					antagonists of the invention)	adipocyte activation. An
					include the assays disclosed in	alternative highly preferred
Clin					Forrer et al., Biol Chem 379(8-	embodiment of the invention
					9):1101-1110 (1998); Le	includes a method for inhibiting
					Marchand-Brustel Y, Exp Clin	the activation of (e.g.,
					Endocrinol Diabetes	decreasing) and/or inactivating
					107(2):126-132 (1999);	adipocytes. Highly
					Kyriakis JM, Biochem Soc	preferred indications include

											_																		
endocrine disorders (e.g., as described below under "Endocrine Disorders").	Highly preferred indications	also include neoplastic diseases	and/or as described below under	"Hyperproliferative Disorders").	Preferred indications include	blood disorders (e.g.,	hypertension, congestive heart	failure, blood vessel blockage,	heart disease, stroke, impotence	and/or as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity		and infection (e.g., as described	below under "Infectious	Disease"). A highly	preferred indication is diabetes	mellitus. An additional	highly preferred indication is a	complication associated with	diabetes (e.g., diabetic	retinopathy, diabetic	nephropathy, kidney disease
Symp 64:29-48 (1999); Chang and Karin, Nature	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of winch	reference in its entirety. Mouse	adipocyte cells that may be used	according to these assays are	publicly available (e.g., through	the ATCC). Exemplary mouse	adipocyte cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1 is	an adherent mouse preadipocyte	cell line that is a continuous	substrain of 3T3 fibroblast cells	developed through clonal	isolation and undergo a pre-	adipocyte to adipose-like	conversion under appropriate	differentiation conditions known	in the art.									
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(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section	below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,	neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma,	heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine	disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below

(particularly of the urinary tract and skin). An additional highly preferred indication is	obesity and/or complications associated with obesity.	Additional highly preferred indications include weight loss	or alternatively, weight gain.	Additional highly preferred indications	associated with insulin	resistance. Additional	highly preferred indications are disorders of the musculoskeletal	systems including myopathies,	muscular dystrophy, and/or as	described herein. Additional	highly preferred indications	include, hypertension, coronary	artery disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia, and	kidney diseases or disorders.	Preferred indications include	neoplasms and cancer, such as,	lymphoma, leukemia and breast,	colon, and kidney cancer.	Additional preferred indications	include melanoma, prostate,	lung, pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Highly preferred
		and the second s																						-		

i					indications include lipomas and
		,			liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HDPFF10	495	Production of	MIP-1alpha FMAT. Assays for	A highly preferred
~1) }	MIPlaipha	immunomodulatory proteins	embodiment of the invention
				produced by activated dendritic	includes a method for
				cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well known	embodiment of the invention
				in the art and may be used or	includes a method for inhibiting
				routinely modified to assess the	(e.g., reducing) MIP1a
				ability of polypeptides of the	production. A highly
				invention (including antibodies	preferred indication is infection
				and agonists or antagonists of	(e.g., an infectious disease as
				the invention) to mediate	described below under
				immunomodulation, modulate	"Infectious Disease").
				chemotaxis, and modulate T cell	Preferred indications include
				differentiation. Exemplary	blood disorders (e.g., as
				assays that test for	described below under "Immune
				immunomodulatory proteins	Activity", "Blood-Related
				evaluate the production of	Disorders", and/or
				chemokines, such as	"Cardiovascular Disorders").
		_		macrophage inflammatory	Highly preferred indications
				protein 1 alpha (MIP-1a), and	include autoimmune diseases
				the activation of	(e.g., rheumatoid arthritis,
				monocytes/macrophages and T	systemic lupus erythematosis,
				cells. Such assays that may be	multiple sclerosis and/or as
				used or routinely modified to	described below) and

immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy.	Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach,
chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp	Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to	these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.

		invention) to mediate	imminodefficiencies (e.g., as
		immunomodulation and	described below). Highly
		differentiation and modulate T	preferred indications also
		cell proliferation and function.	include boosting a B cell-
		Exemplary assays that test for	mediated immune response and
		immunomodulatory proteins	alternatively suppressing a B
		evaluate the production of	cell-mediated immune response.
		cytokines, such as IL-6, and the	Highly preferred indications
	-	stimulation and upregulation of	include inflammation and
		T cell proliferation and	inflammatory
		functional activities. Such	disorders.Additional highly
		assays that may be used or	preferred indications include
		routinely modified to test	asthma and allergy. Highly
		immunomodulatory and	preferred indications include
		diffferentiation activity of	neoplastic diseases (e.g.,
		polypeptides of the invention	myeloma, plasmacytoma,
		(including antibodies and	leukemia, lymphoma,
		agonists or antagonists of the	melanoma, and/or as described
		invention) include assays	below under "Hyperproliferative
		disclosed in Miraglia et al., J	Disorders"). Highly preferred
		Biomolecular Screening 4:193-	indications include neoplasms
		204(1999); Rowland et al.,	and cancers, such as, myeloma,
		"Lymphocytes: a practical	plasmacytoma, leukemia,
		approach" Chapter 6:138-160	lymphoma, melanoma, and
		(2000); and Verhasselt et al., J	prostate, breast, lung, colon,
		Immunol 158:2919-2925	pancreatic, esophageal, stomach,
		(1997), the contents of each of	brain, liver and urinary cancer.
		which are herein incorporated	Other preferred indications
		by reference in its entirety.	include benign dysproliferative
		Human dendritic cells that may	disorders and pre-neoplastic
		be used according to these	conditions, such as, for example,
		assays may be isolated using	hyperplasia, metaplasia, and/or
		techniques disclosed herein or	dysplasia. Preferred indications

include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infectious disease as described below under "Infectious Disease").	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g.,
otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate gene
	Activation of transcription through GAS response element in immune cells (such as eosinophils).
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rheumatoid arthritis, systemic	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting an	eosinophil-mediated immune	response and, alternatively,	suppressing an eosinophil-	mediated immune response.																							
expression (commonly via	involved in a wide variety of	cell functions. Exemplary	assays for transcription through	the GAS response element that	may be used or routinely	modified to test GAS-response	element activity of polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by reference	in its entirety. Moreover,	exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to activate or inhibit
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			•	•										_								_									

activation of immune cells	include assays disclosed and/or	cited in: Mayumi M., "EoL-1, a	human eosinophilic cell line"	Leuk Lymphoma; Jun;7(3):243-	50 (1992); Bhattacharya S,	"Granulocyte macrophage	colony-stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol	Chem; Oct 20;275(42):33167-	75 (2000); the contents of each	of which are herein incorporated	by reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are a type of	immune cell important in the	late stage of allergic reactions;	they are recruited to tissues and	mediate the inflammtory	response of late stage allergic	reaction. Increases in GAS	mediated transcription in	eosinophils is typically a result
						and the same of th								_																		

					of STAT activation, normally a	
HDPFU43 496 Activation of Kinase assay. Kinase assays. Skeletal Mucle Cell for example an CSK-3 kinase P13 Kinase Signalling Pathway transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies an	_				direct consequence of	
HDPFU43 496 Activation of Kinase assay. Kinase assays, Skeletal Mucle Cell for example an GSK-3 kinase P13 Kinase Signalling Pathway transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survivial. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase activity that may be used or routinely modified to test P13 kinase activity that may be used or routinely modified to test P13 kinase activity that may be used or routinely modified to test P13 kinase activity assays for P13 kinase activity in the invention include assays disclosed in Forrer et al., Biol (1998). Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the					interleukin or other cytokine	
HDPFU43 496 Activation of Kinase assay, Kinase assays, Skeletal Mucle Cell Skeletal Mucle Cell Grexample an GSK-3 kinase signal Signalling Pathway transduction that regulate plucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase activity that may be used or routinely modified to test P13 kinase activity and field to test P13 kinase activity and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or					receptor stimulation (e.g. IL3,	
HDPFU43 496 Activation of Kinase assay. Kinase assays, Skeletal Mucle Cell for example an GSK-3 kinase P13 Kinase Signalling Pathway transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase activity that may be used or routinely modified to test P13 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists or antag					IL5 or GMCSF).	
Skeletal Mucle Cell for example an GSK-3 kinase P13 Kinase P13 Kinase Signal Ing Pathway glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase activity that may be used or routinely modified to test P13 kinase activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention (1998), Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the		HDPFU43	496	Activation of	Kinase assay. Kinase assays,	A highly preferred
assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the	82			Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the				PI3 Kinase	assay, for PI3 kinase signal	includes a method for increasing
glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the				Signalling Pathway	transduction that regulate	muscle cell survival An
				,	glucose metabolism and cell	alternative highly preferred
of on the or of					survivial are well-known in the	embodiment of the invention
of or or on O);					art and may be used or routinely	includes a method for
or on O);					modified to assess the ability of	decreasing muscle cell survival.
or on (c)					polypeptides of the invention	A preferred embodiment of the
					(including antibodies and	invention includes a method for
					agonists or antagonists of the	stimulating muscle cell
					invention) to promote or inhibit	proliferation. In a specific
					glucose metabolism and cell	embodiment, skeletal muscle
	·				survival. Exemplary assays for	cell proliferation is stimulated.
_					PI3 kinase activity that may be	An alternative highly preferred
_					used or routinely modified to	embodiment of the invention
					test PI3 kinase-induced activity	includes a method for inhibiting
· • • • • • • • • • • • • • • • • • • •					of polypeptides of the invention	muscle cell proliferation. In a
· · · · · · · · · · · · · · · · · · ·					(including antibodies and	specific embodiment, skeletal
;;					agonists or antagonists of the	muscle cell proliferation is
÷					invention) include assays	inhibited. A preferred
0);					disclosed in Forrer et al., Biol	embodiment of the invention
0);					Chem 379(8-9):1101-1110	includes a method for
0);					(1998); Nikoulina et al.,	stimulating muscle cell
					Diabetes 49(2):263-271 (2000);	differentiation. In a specific
					and Schreyer et al., Diabetes	embodiment, skeletal muscle
					48(8):1662-1666 (1999), the	cell differentiation is stimulated.

		contents of each of which are	An alternative highly preferred
		herein incomprated by reference	embodiment of the invention
		in its entirety. Rat myoblast	includes a method for inhibiting
	-	cells that may be used according	muscle cell differentiation. In a
		to these assays are publicly	specific embodiment, skeletal
		available (e.g., through the	muscle cell differentiation is
		ATCC). Exemplary rat	inhibited. Highly preferred
		 myoblast cells that may be used	indications include disorders of
		according to these assays	the musculoskeletal system.
		 include L6 cells. L6 is an	Preferred indications include
		adherent rat myoblast cell line,	neoplastic diseases (e.g., as
		isolated from primary cultures	described below under
		of rat thigh muscle, that fuses to	"Hyperproliferative Disorders"),
		form multinucleated myotubes	endocrine disorders (e.g., as
		and striated fibers after culture	described below under
-		in differentiation media.	"Endocrine Disorders"), neural
			disorders (e.g., as described
			below under "Neural Activity
			and Neurological Diseases"),
			blood disorders (e.g., as
			described below under "Immune
			Activity", "Cardiovascular
			Disorders", and/or "Blood-
			Related Disorders"), immune
			disorders (e.g., as described
			below under "Immune
			Activity"), and infection (e.g., as
			described below under
			"Infectious Disease"). A
			highly preferred indication is
			diabetes mellitus. An
	-		additional highly preferred
			indication is a complication

associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section	below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel blockage), seizures, mental	contusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular	Disorders" section below), dyslipidemia, endocrine disorders (as described in the	below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness),	ulcers and impaired wound healing, infections (e.g.,
								<u> </u>		

infectious diseases and disorders	Diseases" section below,	especially of the urinary tract	and skinly, carpar tunner syndrome and Dupuytren's	contracture). An additional	highly preferred indication is	obesity and/or complications	associated with obesity.	Additional highly preferred	indications include weight loss	or alternatively, weight gain.	Additional highly preferred	indications are complications	associated with insulin	resistance. Additonal	highly preferred indications are	disorders of the musculoskeletal	system including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and vascular	disease. Highly preferred	indications include neoplasms	and cancer, such as,

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rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described
	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor
	Production of TNF alpha by dendritic cells
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below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated	immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating ioint damage in patients	with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include			lymphoma, melanoma, glloma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include henion dysproliferative	
necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to	test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204(1999); Rowland et al., "Lymphocytes: a practical	approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890	(1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its	entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed	the art. Human dendritic cells are antigen presenting cells in
	·						

indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Immune Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving T-cells). Highly preferred embodiments of the invention include methods of
activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may
	CD152 in Human T
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	HDPFY18
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preventing, detecting, diagnosing.	treating and/or ameliorating	disorders of the immune system	(particularly including, but not	limited to, immune disorders	invoiving i-cells).																									
lead to impaired pre	es. Assays for	immunomodulatory proteins dis	important in the maintenance (pa		expressed almost exclusively	on CD4+ and CD8+ T cells are	well known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to modulate the	activation of T cells, maintain	T cell homeostasis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the upregulation of	cell surface markers, such as	CD152, and the activation of T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include, for	example, the assays disclosed
												•																		
															-															

				in Miraglia et al., J	
	·			Biomolecular Screening 4:193-	
				204 (1999); Rowland et al.,	
				"Lymphocytes: a practical	
				approach" Chapter 6:138-160	
				(2000); McCoy et al., Immunol	
				Cell Biol 77(1):1-10 (1999);	
				Oostervegal et al., Curr Opin	
				Immunol 11(3):294-300	
				(1999); and Saito T, Curr Opin	
				Immunol 10(3):313-321	
				(1998), the contents of each of	
				which are herein incorporated	
				by reference in its entirety.	
				Human T cells that may be	
				used according to these assays	
				may be isolated using	
				techniques disclosed herein or	
				otherwise known in the art.	
				Human T cells are primary	
				human lymphocytes that	
				mature in the thymus and	
				express a T Cell receptor and	
				CD3, CD4, or CD8. These	
				cells mediate humoral or cell-	
				mediated immunity and may	
				be preactivated to enhance	
				responsiveness to	
				immunomodulatory factors.	
	HDPFY18	497	Activation of	Assays for the activation of	Highly preferred indications
83			transcription through	transcription through the NFKB	include inflammation and

NFKB response	response element are well-	inflammatory disorders.
element in immune	known in the art and may be	Highly preferred indications
 cells (such as T-	used or routinely modified to	include blood disorders (e.g., as
cells).	assess the ability of	described below under "Immune
	polypeptides of the invention	Activity", "Blood-Related
	(including antibodies and	Disorders", and/or
	agonists or antagonists of the	"Cardiovascular Disorders").
	invention) to regulate NFKB	Highly preferred indications
	transcription factors and	include autoimmune diseases
 	modulate expression of	(e.g., rheumatoid arthritis,
	immunomodulatory genes.	systemic lupus erythematosis,
	Exemplary assays for	multiple sclerosis and/or as
-	transcription through the NFKB	described below), and
	response element that may be	immunodeficiencies (e.g., as
	used or rountinely modified to	described below). An additional
	test NFKB-response element	highly preferred indication is
	activity of polypeptides of the	infection (e.g., AIDS, and/or an
	invention (including antibodies	infectious disease as described
 -	and agonists or antagonists of	below under "Infectious
	the invention) include assays	Disease"). Highly preferred
	disclosed in Berger et al., Gene	indications include neoplastic
	66:1-10 (1998); Cullen and	diseases (e.g., melanoma,
	Malm, Methods in Enzymol	leukemia, lymphoma, and/or as
	216:362-368 (1992); Henthorn	described below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative Disorders").
	85:6342-6346 (1988); Black et	Highly preferred indications
	al., Virus Gnes 15(2):105-117	include neoplasms and cancers,
	(1997); and Fraser et al.,	such as,melanoma, renal cell
	29(3):838-844 (1999), the	carcinoma, leukemia,
	contents of each of which are	lymphoma, and prostate, breast,
	herein incorporated by reference	lung, colon, pancreatic,
	in its entirety. T cells that may	esophageal, stomach, brain,
	be used according to these	liver and urinary cancer. Other

preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,	sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity",
assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension	culture of 1L-2 and 1L-4 responsive T cells.		Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
			Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
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			HDPIE44
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	agonists or antagonists of the	and "Blood-Related Disorders"),
	invention) to promote or inhibit	autoimmune diseases (e.g.,
	cell proliferation, activation, and	rheumatoid arthritis, systemic
	apoptosis. Exemplary assays for	lupus erythematosis, Crohn"s
	JNK kinase activity that may be	disease, multiple sclerosis
	used or routinely modified to	and/or as described below),
	test JNK kinase-induced activity	immunodeficiencies (e.g., as
	of polypeptides of the invention	described below). Highly
	(including antibodies and	preferred indications also
	agonists or antagonists of the	include boosting or inhibiting
	invention) include the assays	immune cell proliferation.
	disclosed in Forrer et al., Biol	Preferred indications include
	Chem 379(8-9):1101-1110	neoplastic diseases (e.g.,
	(1998); Gupta et al., Exp Cell	leukemia, lymphoma, and/or as
	Res 247(2): 495-504 (1999);	described below under
	Kyriakis JM, Biochem Soc	"Hyperproliferative Disorders").
	Symp 64:29-48 (1999); Chang	Highly preferred indications
	and Karin, Nature	include boosting an eosinophil-
	410(6824):37-40 (2001); and	mediated immune response, and
	Cobb MH, Prog Biophys Mol	suppressing an eosinophil-
	Biol 71(3-4):479-500 (1999);	mediated immune response.
	the contents of each of which	
	are herein incorporated by	
	reference in its entirety.	
	Exemplary cells that may be	
	used according to these assays	
	include eosinophils.	
	Eosinophils are important in the	
	late stage of allergic reactions;	
	they are recruited to tissues and	
	mediate the inflammatory	
	response of late stage allergic	
	reaction. Moreover, exemplary	

assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include	assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone- induced apoptosis and activation	of c-Jun NH2-terminal Kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000);	Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep:104(3 Pt 1):565-74:	and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase	phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-

HDPILI94	400	SEAP in 3T31.1	74 (1999); the contents of each of which are herein incorporated by reference in its entirety. Assays for the regulation (i.e.	Diabetes
	2	SEAF III 3 1 3 L1	increases or decreases) of viability and proliferation of cells in vitro are well-known in the art	A highly preferred indication is diabetes. Additional highly preferred indications include
			and may be used or routinely modified to assess the ability of	complications associated with diabetes (e.g., diabetic
			polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases
			regulate viability and proliferation of preadipose cells	and disorders as described in the "Renal Disorders" section below),
			and cell lines. For example, the CellTiter-Glo TM Luminescent	diabetic neuropathy, nerve disease and nerve damage (e.g.,
			Cell Viability Assay (Promega Corp., Madison, WI, USA) can be	due to diabetic neuropathy), blood vessel blockage, heart
-			used to measure the number of viable cells in culture based on	disease, stroke, impotence (e.g., due to diabetic neuropathy or
			quantitation of the ATP present which signals the presence of	blood vessel blockage), seizures, mental confusion, drowsiness,
			metabolically active cells. Adjuncates and pre-adjuncates	nonketotic hyperglycemic-
			that may be used according to	cardiovascular disease (e.g., heart
			these assays are publicly available (e.g., through the ATCC) and/or	disease, atherosclerosis, microvascular disease,
			may be routinely generated.	hypertension, stroke, and other
			according to these assays include	described in the "Cardiovascular
			the mouse 3T3-L1 cell line which	Disorders" section below),
			Is an adherent mouse	dyslipidemia, endocrine disorders
			continuous substrain of 3T3	Disorders" section below),

nmpairment hopathy and and impaired d infection seases and bed in the es" section of the urinary ighly preferred clude obesity, veight loss, as ons associated ht gain, and rired invention f preventing, ing, treating g the above ons, disorders,	erred stes mellitus. hly preferred nplication labetes (e.g., hy, diabetic ley disease i, nephropathy lses and libed in the lsection leuropathy,
neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin). Highly preferred indications also include obesity, weight gain, and weight loss, as well as complications associated with obesity, weight gain, and embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating the above mentioned conditions, disorders, and diseases.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy,
fibroblast cells developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions. Cells were differentiated to an adipose-like state before being used in the screen. See, Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis.
	Regulation of transcription of Malic Enzyme in hepatocytes
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	HDPIU94
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(e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropainy or oroog vesser blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders" section below),	disorders (as described in the "Endocrine Disorders" section	below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness),	healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious	Diseases" section below, especially of the urinary tract and skin), carpal tunnel	syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications
stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as	putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors.	Exemplary assays that may be used or routinely modified to test for regulation of transcription of Malic Enzyme	(in hepatocytes) by polypeptides of the invention (including	antibodies and agonists or antagonists of the invention)	Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91	al., Mol Endocrinol, 8(10):1361-9 (1994); Barroso, I., et al., J	Biol Chem, 274(23):17997-6004 (1999); Ijpenberg, A., et al., J Biol Chem, 272(32):20108- 20117 (1997); Berger, et al.,	Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992),	the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these

associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include asthma, allergy, hypersensitivity reactions, and inflammation. Preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), immunological disorders, inflammation and inflammatory disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid
assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the mouse 3T3-L1 cell line. 3T3-L1 is a mouse preadipocyte cell line (adherent). It is a continuous substrain of 3T3 fibroblasts developed through clonal isolation. Cells undergo a preadipocyte to adipose-like conversion under appropriate differentiation culture conditions.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be
	Activation of transcription through NFKB response element in immune cells (such as EOL1 cells).
	499
	HDPIU94
	88

arthritis, systemic lupus erythematosis, multiple sclerosis	immunodeficiencies (e.g., as	described below).																												
used or rountinely modified to art test NFKB-response element ery			the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety. For	example, a reporter assay	(which measures increases in	transcription inducible from a	NFkB responsive element in	EOL-1 cells) may link the	NFKB element to a repeorter	gene and binds to the NFKB	transcription factor, which is	upregulated by cytokines and	other factors. Exemplary	immune cells that may be used	according to these assays	include eosinophils such as the
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	A highly preferred embodiment of the invention includes a method for stimulating hepatocyte cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting hepatocyte cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating hepatocyte cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting hepatocyte cell differentiation. A highly preferred embodiment of the invention includes a method for activating hepatocyte cells. An alternative highly preferred embodiment of the invention includes a method for activating hepatocyte cells. An alternative highly preferred embodiment of the invention
human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in
	Activation of Hepatocyte ERK Signaling Pathway
	499
	HDPIU94
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the activation of and/or inactivating hepatocyte cells. Highly preferred indications include disorders of the liver and/or endocrine disorders (e.g.,	as described below under "Endocrine Disorders"). Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as	Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and	Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy (e.g., renal failure, nephropathy
9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys	Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Rat liver hepatoma cells that may be used according to these assays are publicly available (e.g.,	rat liver hepatoma cells that may be used according to these assays include H4lle cells, which are known to respond to glucocorticoids, insulin, or cAMP derivatives.	

and/or other diseases and disorders as described in the "Renal Disorders" section	below), diabetic neuropathy, nerve disease and nerve damage	neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel	blockage), seizures, mental confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dysupidemia, endocrine disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, infection (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract
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and skin), carpal tunnel syndrome and Dupuytren's	contracture). An additional	highly preferred indication is	obesity and/or complications	associated with obesity.	Additional highly preferred	indications include weight loss	or alternatively, weight gain.	Additional highly preferred	indications are complications	associated with insulin	resistance. Additonal	highly preferred indications are	disorders of the musculoskeletal	systems including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include, hepatitis,	jaundice, gallstones, cirrhosis of	the liver, degenerative or	necrotic liver disease, alcoholic	liver diseases, fibrosis, liver	regeneration, metabolic disease,	dyslipidemia and chlolesterol	metabolism.	Additional highly preferred	indications include neoplasms	and cancers, such as,	hepatocarcinomas, other liver	cancers, and colon and	pancreatic cancer. Preferred
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indications also include prostate, breast, lung, esophageal, stomach, brain, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
	Kinase assays, for example an Elk-1 kinase assay for ERK signal transduction that regulates cell proliferation or differentiation, are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Ali H, et al., J
	Regulation of proliferation and/or differentiation in immune cells (such as mast cells).
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	HDPIU94
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	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
(2000); Tam SY, et al., Blood, 90(5):1807-1820 (1997); Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Berra et al., Biochem Pharmacol 60(8):1171-1178 (2000); Gupta et al., Exp Cell Res 247(2):495-504 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells that may be used according to these assays include human mast cells such as the HMC-1 cell line.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and
	Production of IFNgamma using a T cells
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	HDPIU94
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"Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis,	infections associated with chronic granulomatosus disease	and malignant osteoporosis,	"Infectious Disease"). Highly	preferred indications include	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency (e.g.,	as described below), boosting a	T cell-mediated immune	response, and suppressing a T	cell-mediated immune response.	Additional highly preferred	indications include	inflammation and inflammatory	disorders. Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,
inhibit TH2 helper cell functions are well known in the art and	modified to assess the ability of	(including antibodies and	agonists or antagonists of the invention) to mediate	immunomodulation, regulate	inflammatory activities, modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for immunomodulatory	proteins evaluate the production	of cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);
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melanoma, and prostate, breast,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma and allergy.			-	
Billiau et al., Ann NY Acad Sci	Annu Rev Immunol 15:749-795	(1997), and Rheumatology	(Oxford) 38(3):214-20 (1999),	the contents of each of which	are herein incorporated by	reference in its entirety. Human	T cells that may be used	according to these assays may	be isolated using techniques	disclosed herein or otherwise	known in the art. Human T	cells are primary human	lymphocytes that mature in the	thymus and express a T Cell	receptor and CD3, CD4, or	CD8. These cells mediate	humoral or cell-mediated	immunity and may be	preactivated to enhance	responsiveness to	immunomodulatory factors.						RANTES FMAT. Assays for	immunomodulatory proteins	that induce chemotaxis of 1	cells, monocytes, and
																											Production of	RANTES in	endothelial cells	(such as human
																											500			
																					-						HDPOL37			
																						-						98		

eosinophils are well known in	the art and may be used or	routinely modified to assess the	ability of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to mediate	immunomodulation, induce	chemotaxis, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for immunomodulatory	proteins evaluate the production	of cytokines, such as RANTES,	and the induction of chemotactic	responses in immune cells.	Such assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of
umbilical vein	endothelial cells	(HUVEC))																														
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	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),
which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	SRE) are tr and may modified to modified to s and ss and sts of the te serum I modulate nes involved culate the related genes Exemplary
which are here by reference Endothelial used accordance are publicly through the endothelial used according which are which line and are invested and are invested to, angioge permeabili immune ce	Activation of Assays for the activa transcription through serum response element in immune cells (such as natural killer cells). killer cells). polypeptides of the including antibodie agonists or antagoni invention) to regular response factors and the expression of ge in growth and upregundant cell types.
	500 Activations transc serum eleme cells (killer
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Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic rupus erymematosis, Crohn's disease, multiple sclerosis and/or as described	below), immunodeficiencies (e.g.; as described below),	boosting a 1 cell-mediated immune response, and	suppressing a 1 cell-mediated immune response. Additional	highly preferred indications	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include		leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for		melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,
assays for transcription through the SRE that may be used or routinely modified to test SRE	activity of the polypeptides of the invention (including antibodies and agonists or	antagonists of the invention) include assays disclosed in	Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	Methods in Enzymol 216:362- 368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1968); Delison et al., I Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary T cells that	may be used according to these	assays include the NK-YT cell	line, which is a human natural	killer cell line with cytolytic and	cytotoxic activity.				
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					liver and urinary cancer. Other
					preferred indications include
			-		benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for example,
					hyperplasia, metaplasia, and/or
					dysplasia. Preferred
					indications include anemia,
					pancytopenia, leukopenia,
					thrombocytopenia, Hodgkin's
					disease, acute lymphocytic
					anemia (ALL), plasmacytomas,
					multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
-					neutropenia, neutrophilia,
					psoriasis, suppression of
					immune reactions to
					transplanted organs and tissues,
					hemophilia, hypercoagulation,
			-		diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication is
					infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HDP0076	501	Activation of	Assays for the activation of	A preferred embodiment of
87			transcription through	transcription through the Serum	the invention includes a method
			serum response	Response Element (SRE) are	for inhibiting (e.g., reducing)

well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T				1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	_
such as T- assess the ability of assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362- 368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105- 117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T		element in immune	well-known in the art and may	I NF alpha production. An	
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T		cells (such as T-	be used or routinely modified to	alternative preferred	
including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T		cells).	assess the ability of	embodiment of the invention	
im im ling ling ling			polypeptides of the invention	includes a method for	
			(including antibodies and	stimulating (e.g., increasing)	
			agonists or antagonists of the	TNF alpha production.	
<u> </u>			invention) to regulate the serum	Preferred indications include	
			response factors and modulate	blood disorders (e.g., as	
M = b0 b			the expression of genes involved	described below under "Immune	
			in growth. Exemplary assays	Activity", "Blood-Related	
e e e			for transcription through the	Disorders", and/or	
g eq c			SRE that may be used or	"Cardiovascular Disorders"),	
g g eq	-		routinely modified to test SRE	Highly preferred indications	
ck ck			activity of the polypeptides of	include autoimmune diseases	
2- lack 5- 5- 5- 7 T ding			the invention (including	(e.g., rheumatoid arthritis,	
2- lack 5- 5- ated T ding	-	-	antibodies and agonists or	systemic lupus erythematosis,	
2- lack lack ch the the the the the the the the the th			antagonists of the invention)	Crohn"s disease, multiple	
62- Black 35- each orated T ording			include assays disclosed in	sclerosis and/or as described	
362- ., Black 05- each orated . T ording y		_	Berger et al., Gene 66:1-10	below), immunodeficiencies	
			(1998); Cullen and Malm,	(e.g., as described below),	
		-	Methods in Enzymol 216:362-	boosting a T cell-mediated	
			368 (1992); Henthorn et al.,	immune response, and	
			Proc Natl Acad Sci USA	suppressing a T cell-mediated	
			85:6342-6346 (1988); and Black	immune response. Additional	
			et al., Virus Genes 12(2):105-	highly preferred indications	
			117 (1997), the content of each	include inflammation and	
			of which are herein incorporated	inflammatory disorders, and	
gu gu			by reference in its entirety. T	treating joint damage in patients	
T.			cells that may be used according	with rheumatoid arthritis. An	
T.	_		to these assays are publicly	additional highly preferred	
			available (e.g., through the	indication is sepsis. Highly	
_			ATCC). Exemplary mouse T	preferred indications include	
-			cells that may be used according	neoplastic diseases (e.g.,	\neg

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1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	leukemia, lympnoma, and/or as	described below under	whyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophilia,	psoriasis, suppression of	immune reactions to	transplanted organs and tissues,	hemophilia, hypercoagulation,
	to these assays include the	CTLL cell line, which is an IL-2	dependent suspension culture of	T cells with cytotoxic activity.																													
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diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Diabetes A highly preferred indication is diabetes. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthase, the first specific enzyme in the cholesterol biosynthetic pathway (G. Jiang, T. L. McKenzie, D. G. Conrad, and I. Shechter. Transcriptional Regulation by Lovastatin and 25-Hydroxycholesterol in HepG2 Cells and Molecular Cloning and Expression of the cDNA for the Human Hepatic Squalene Synthase. J. Biol. Chem. 268:12818-12824, 1993). Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). Knowles BB, Howe CC, Aden DP. Human hepatocellular
	SEAP in HepG2/Squale- synthetase(stimulati on)
	501
	HDPO076
	87

described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin). Highly preferred indications also include obesity, weight gain, and weight loss, as well as complications associated with obesity, weight gain, and weight loss. Preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating the above mentioned conditions, disorders, and diseases.	
DP. Human hepatocellular carcinoma cell lines secrete the major plasma proteins and hepatitis B surface antigen. Science. 209:497-9,1980.	Kinase assay: measures the phosphorylation of Elk-1, an indication of activation of extracellular signal regulated kinase (ERK). ERK pathway regulates cell growth, proliferation and differentiation. Cells were pretreated with SID supernatants for 15-18 hours,
	Inhibition of adipocyte ERK signaling pathway.
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	Н DРРD93
	88

		A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An
and then 100 nM of insulin was added to stimulate ERK kinase. Phosphorylation of Elk-1 was measured after a 20 minute incubation. Pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. Cells were differentiated to an adipose-like state before being used in the screen. See Green et al., Cell 3: 127-133 (1974), the	incorporated by reference in its entirety.	Kinase assay. Kinase assays, for example an GSK-3 assays, for P13 kinase signal transduction that regulate
		Activation of Adipocyte PI3 Kinase Signalling Pathway
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alternative highly preferred embodiment of the invention includes a method for	decreasing adipocyte survival. A preferred embodiment of the invention includes a method for	stimulating adipocyte proliferation. An alternative highly preferred embodiment of	the invention includes a method for inhibiting adipocyte proliferation. A preferred	embodiment of the invention includes a method for	stimulating adipocyte differentiation. An alternative	highly preferred embodiment of the invention includes a method	for inhibiting adipocyte	preferred indications include	endocrine disorders (e.g., as described below under	"Endocrine Disorders").	Preferred indications include	neoplastic diseases (e.g., linomas, linosarcomas, and/or as		"Hyperproliferative Disorders"),			failure, blood vessel blockage, heart disease, stroke, impotence
glucose metabolism and cell survival are well-known in the art and may be used or routinely	modified to assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell	survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to	test PI3 kinase-induced activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) include assays disclosed in Forrer et al Biol	Chem 379(8-9):1101-1110	Diabetes 49(2):263-271 (2000);	and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the	contents of each of which are	herein incorporated by reference	in its entirety. Mouse adipocyte cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary mouse	adipocyte cells that may be used	according to these assays include 3T3-L1 cells. 3T3-L1 is
				· · · · · · · · · · · · · · · · · · ·													

	an adherent mouse preadipocyte	and/or as described below under "Immine Activity"
	substrain of 3T3 fibroblast cells	"Cardiovascular Disorders",
	developed through clonal	and/or "Blood-Related
	isolation and undergo a pre-	Disorders"), immune disorders
	adipocyte to adipose-like	(e.g., as described below under
	conversion under appropriate	"Immune Activity"), neural
	differentiation conditions known	disorders (e.g., as described
	in the art.	below under "Neural Activity
1		and Neurological Diseases"),
		and infection (e.g., as described
		er "In
		Disease"). A highly
		ndicat
		mellitus. An additional
		highly preferred indication is a
		complication associated with
		diabetes (e.g., diabetic
		retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure, nephropathy
		and/or other diseases and
		disorders as described in the
		"Renal Disorders" section
		below), diabetic neuropathy,
		nerve disease and nerve damage
		(e.g, due to diabetic
		neuropathy), blood vessel
		blockage, heart disease, stroke,
		impotence (e.g., due to diabetic
		neuropathy or blood vessel
		blockage), seizures, mental
		confusion, drowsiness,

nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, infection (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract	and skin), carpal tunnel	syndrome and Dupuytren's	contracture). An additional	highly preferred indication is	obesity and/or complications	associated with obesity.	Additional highly preferred	indications include weight loss	or alternatively, weight gain.	Additional highly preferred	indications are complications	associated with insulin
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					highly preferred indications are disorders of the musculoskeletal systems including myopathies,
					highly preferred indications are disorders of the musculoskeletal systems including myopathies,
					disorders of the musculoskeletal systems including myopathies,
					systems including myopathies,
					muscular dystrophy, and/or as
					described herein.
					Additional highly preferred
					indications include,
					hypertension, coronary artery
					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia, and
					kidney diseases or disorders.
					Highly preferred indications
					include neoplasms and cancer,
					such as, lipoma, liposarcoma,
					lymphoma, leukemia and breast,
					colon, and kidney cancer.
		• • • •			Additional highly preferred
					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
100					conditions, such as, for example,
					hyperplasia, metaplasia, and/or
					dysplasia.
	HDPPD93	502	Activation of	Assays for the activation of	Preferred indications include
88			hrough	transcription through the AP1	neoplastic diseases (e.g., as

				these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the HT2 cell line, which is an IL-2 dependent suspension culture cell line that also responds to IL-4.	include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
88	Н DPPD93	502	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as

described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred	indications include inflammatory disorders. An additional highly preferred indication is infection	(e.g., an intectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include	neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to	test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer	et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993),	the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the	ALCC). Exemplary numan INK cells that may be used according to these assays include the NK-

		-	YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HDPPD93	502	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as

HDPPD93 5	502	Activation of transcription through CD28 response element in immune cells (such as T.	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to	psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease. A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred
		cells).	assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. An alternative highly preferred
			et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra	indications include inflammatory disorders. Highly preferred indications include autoimmune

diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below),	immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response,	and suppressing a 1 cell- mediated immune response. Highly preferred indications	include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as	described below under "Hyperproliferative Disorders").	Highly preferred indications include neoplasms and cancers,	such as, for example, melanoma	(e.g., metastatic melanoma), renal cell carcinoma (e.g.,	metastatic renal cell carcinoma),	cell lymphoma), and prostate,	breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. A highly preferred indication includes infection
et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of	which are herein incorporated by reference in its entirety. T cells that may be used according	to these assays are publicly available (e.g., through the ATCC). Exemplary human T	cells that may be used according to these assays include the SUPT cell line, which is a	suspension culture of IL-2 and IL-4 responsive T cells.	•											
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(e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression	transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related	Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
	·		

					asthma and allergy.
	HDPPD93	502	Activation of	Assays for the activation of	Highly preferred indications
88			transcription through	transcription through the	include blood disorders (e.g., as
)			NFAT response	Nuclear Factor of Activated T	described below under "Immune
			element in immune	cells (NFAT) response element	Activity", "Blood-Related
			cells (such as T-	are well-known in the art and	Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
			`	modified to assess the ability of	Highly preferred indications
				polypeptides of the invention	include autoimmune diseases
				(including antibodies and	(e.g., rheumatoid arthritis,
				agonists or antagonists of the	systemic lupus erythematosis,
			-12/2	invention) to regulate NFAT	multiple sclerosis and/or as
				transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in immunomodulatory	described below), boosting a T
				functions. Exemplary assays for	cell-mediated immune response,
				transcription through the NFAT	and suppressing a T cell-
				response element that may be	mediated immune response.
				used or routinely modified to	Additional highly preferred
				test NFAT-response element	indications include
				activity of polypeptides of the	inflammation and inflammatory
				invention (including antibodies	disorders. An additional highly
				and agonists or antagonists of	preferred indication is infection
				the invention) include assays	(e.g., an infectious disease as
				disclosed in Berger et al., Gene	described below under
				66:1-10 (1998); Cullen and	"Infectious Disease").
				Malm, Methods in Enzymol	Preferred indications include
				216:362-368 (1992); Henthorn	neoplastic diseases (e.g.,
		_		et al., Proc Natl Acad Sci USA	leukemia, lymphoma, and/or as
				85:6342-6346 (1988); Serfling	described below under
				et al., Biochim Biophys Acta	"Hyperproliferative Disorders").
_				1498(1):1-18 (2000); De Boer et	Preferred indications include

				of Int I Biochem Cell Biol	neonlasms and cancers, such as
•				al., IIIC DIOCINAII COI DIOI	for assumpto laukomio
				31(10):1221-1236 (1999);	ior example, leukeiiiia,
				Fraser et al., Eur J Immunol	lymphoma, and prostate, breast,
	•			29(3):838-844 (1999); and	lung, colon, pancreatic,
			-	Yeseen et al., J Biol Chem	esophageal, stomach, brain,
			••	268(19):14285-14293 (1993),	liver and urinary cancer. Other
				the contents of each of which	preferred indications include
				are herein incorporated by	benign dysproliferative
				reference in its entirety. T cells	disorders and pre-neoplastic
				that may be used according to	conditions, such as, for example,
				these assays are publicly	hyperplasia, metaplasia, and/or
				available (e.g., through the	dysplasia. Preferred
		-		ATCC). Exemplary human T	indications also include anemia,
				cells that may be used according	pancytopenia, leukopenia,
				to these assays include the	thrombocytopenia, Hodgkin's
				SUPT cell line, which is a	disease, acute lymphocytic
				suspension culture of IL-2 and	anemia (ALL), plasmacytomas,
				IL-4 responsive T cells.	multiple myeloma, Burkitt's
				•	lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted organs
					and tissues, hemophilia,
					hypercoagulation, diabetes
	-				mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HDPPD93	502	Activation of	Assays for the activation of	Highly preferred indications
88			transcription through	transcription through the NFKB	include inflammation and

inflammatory disorders. Highly preferred indications	include blood disorders (e.g., as	described below under Immune	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An additional	highly preferred indication is	infection (e.g., AIDS, and/or an	infectious disease as described	below under "Infectious	Disease"). Highly preferred	indications include neoplastic	diseases (e.g., melanoma,	leukemia, lymphoma, and/or as	described below under	""("'Hyperproliferative Disorders").	Highly preferred indications	include neoplasms and cancers,	such as, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other
response element are well-known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention finchiding antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the NFKB	response element that may be	used or rountinely modified to	test NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by reference	in its entirety. T cells that may	be used according to these
NFKB response element in immune	cells (such as T-	cells).									_			<u>.</u>			-													
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	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune ibit diseases (e.g., rheumatoid
assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit
	Production of IL-10 and activation of T-cells.
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arthritis, systemic lupus erythematosis, Crohn's disease,	described below),	immunodeficiencies (e.g., as	described below), boosting a 1 cell-mediated immune response,	and suppressing a T cell-	mediated immune response.																								
production of IL-10 and/or activation of T-cells.	Exemplary assays that may be used or routinely modified to	assess the ability of	polypeptides and antibodies of the invention (including agonists	or antagonists of the invention)	to modulate IL-10 production	and/or T-cell proliferation	include, for example, assays	such as disclosed and/or cited	in: Robinson, DS, et al., "Th-2	cytokines in allergic disease" Br	Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the contents	of each of which are herein	incorporated by reference in	their entirety. Exemplary cells	that may be used according to	these assays include Th2 cells.	IL10 secreted from Th2 cells	may be measured as a marker of	Th2 cell activation. Th2 cells	are a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation of	Th2 cells play a major role in
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				the initiation and pathogenesis	
				of allergy and asthma. Primary	
				T helper 2 cells are generated	
				via in vitro culture under Th2	
				polarizing conditions using	
				peripheral blood lymphocytes isolated from cord blood	
08	HDPPW82	503	CD71 in Human T		
	HDPXN20	504	Production of	MIP-1alpha FMAT. Assays for	A highly preferred
06			MIP1alpha	immunomodulatory proteins	embodiment of the invention
))			•	produced by activated dendritic	includes a method for
				cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well known	embodiment of the invention
				in the art and may be used or	includes a method for inhibiting
				routinely modified to assess the	(e.g., reducing) MIP1a
				ability of polypeptides of the	production. A highly
				invention (including antibodies	preferred indication is infection
				and agonists or antagonists of	(e.g., an infectious disease as
				the invention) to mediate	described below under
				immunomodulation, modulate	"Infectious Disease").
				chemotaxis, and modulate T cell	Preferred indications include
				differentiation. Exemplary	blood disorders (e.g., as
				assays that test for	described below under "Immune
				immunomodulatory proteins	Activity", "Blood-Related
				evaluate the production of	Disorders", and/or
				chemokines, such as	"Cardiovascular Disorders").
				macrophage inflammatory	Highly preferred indications
	_			protein 1 alpha (MIP-1a), and	include autoimmune diseases
				the activation of	(e.g., rheumatoid arthritis,
				monocytes/macrophages and T	systemic lupus erythematosis,

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multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Highly preferred indications	include neoplasms and cancers,	such as, leukemia, lymphoma,
cells. Such assays that may be	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and Eremin,	J R Coll Surg Ednb 45(1):9-19	(2001); Drakes et al., Transp	Immunol 8(1):17-29 (2000);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells	that may be used according to	these assays may be isolated	using techniques disclosed	herein or otherwise known in	the art. Human dendritic cells	are antigen presenting cells in	suspension culture, which, when	activated by antigen and/or	cytokines, initiate and
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prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.		
upregulate T cell proliferation and functional activities.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage	activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate
	Production of IFNgamma using a T cells	
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	HDPXN20	
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		inflammatory activities.	autoimmune disease (e.g.,
-		modulate TH2 helper cell	rheumatoid arthritis, systemic
		function, and/or mediate	lupus erythematosis, multiple
		humoral or cell-mediated	sclerosis and/or as described
	-12	immunity. Exemplary assays	below), immunodeficiency (e.g.,
		that test for immunomodulatory	as described below), boosting a
		proteins evaluate the production	T cell-mediated immune
		of cytokines, such as Interferon	response, and suppressing a T
		gamma (IFNg), and the	cell-mediated immune response.
		activation of T cells. Such	Additional highly preferred
		assays that may be used or	indications include
		routinely modified to test	inflammation and inflammatory
		immunomodulatory activity of	disorders. Additional preferred
		polypeptides of the invention	indications include idiopathic
		(including antibodies and	pulmonary fibrosis. Highly
	-	agonists or antagonists of the	preferred indications include
		invention) include the assays	neoplastic diseases (e.g.,
		 disclosed in Miraglia et al., J	leukemia, lymphoma,
		Biomolecular Screening 4:193-	melanoma, and/or as described
		204 (1999); Rowland et al.,	below under "Hyperproliferative
		 "Lymphocytes: a practical	Disorders"). Highly preferred
		approach" Chapter 6:138-160	indications include neoplasms
		 (2000); Gonzalez et al., J Clin	and cancers, such as, for
		 Lab Anal 8(5):225-233 (1995);	example, leukemia, lymphoma,
		Billiau et al., Ann NY Acad Sci	melanoma, and prostate, breast,
		 856:22-32 (1998); Boehm et al.,	lung, colon, pancreatic,
		 Annu Rev Immunol 15:749-795	esophageal, stomach, brain,
		(1997), and Rheumatology	liver and urinary cancer. Other
		(Oxford) 38(3):214-20 (1999),	preferred indications include
		the contents of each of which	benign dysproliferative
		are herein incorporated by	disorders and pre-neoplastic
		 reference in its entirety. Human	conditions, such as, for example,
		T cells that may be used	hyperplasia, metaplasia, and/or

dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in
	Activation of transcription through cAMP response element (CRE) in pre-adipocytes.
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(e.g., renal failure, nephropathy and/or other diseases and	disorders as described in the	"Renal Disorders" section	below), diabetic neuropathy,	nerve disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic	retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g.,	infectious diseases and disorders	as described in the "Infectious	Diseases" section below,
a wide variety of cell functions. For example, a 3T3-L1/CRE	reporter assay may be used to	identify factors that activate the	cAMP signaling pathway.	CREB plays a major role in	adipogenesis, and is involved in	differentiation into adipocytes.	CRE contains the binding	sequence for the transcription	factor CREB (CRE binding	protein). Exemplary assays for	transcription through the cAMP	response element that may be	used or routinely modified to	test cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch et	al., Mol Cell Biol 20(3):1008-	1020 (2000); and Klemm et al.,	J Biol Chem 273:917-923	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. Pre-	adipocytes that may be used
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especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of
	Production of IL-6
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				(2000); and Verhasselt et al., J	prostate, breast, lung, colon,
				(1997), the contents of each of	brain, liver and urinary cancer.
				which are herein incorporated	Other preferred indications
				by reference in its entirety.	include benign dysproliferative
				Human dendritic cells that may	disorders and pre-neoplastic
				be used according to these	conditions, such as, for example,
				assays may be isolated using	hyperplasia, metaplasia, and/or
				techniques disclosed herein or	dysplasia. Preferred indications
				otherwise known in the art.	include anemia, pancytopenia,
				Human dendritic cells are	leukopenia, thrombocytopenia,
				antigen presenting cells in	Hodgkin's disease, acute
				suspension culture, which, when	lymphocytic anemia (ALL),
				activated by antigen and/or	multiple myeloma, Burkitt's
				cytokines, initiate and	lymphoma, arthritis, AIDS,
				upregulate T cell proliferation	granulomatous disease,
				and functional activities.	inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted organs
					and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HDTAU35	505	Production of	MIP-lalpha FMAT. Assays for	A highly preferred
16			MIFIaipna	Immunomonuatory proteins	

cells that upregulate monocyte/macrophage and T cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or includes a method for inhibiting routinely modified to assess the condition. In the art and may be used or includes a method for inhibiting routinely modified to assess the carried and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate T cell differentiation. Exemplary escribed below under "Infectious Disease"). Chemotaxis, and modulate T cell old issorders (e.g., as a sasays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein a lapha (MIP-1a), and the activation of cells. Such assays that may be used or routinely modified to used or routinely modified to used or routinely modified to including antibodies and agonists or antagonists of the invention include assays disclosed in Miragila et al., Biomolecular Screening 4:193-104(1999); Rowland et al., Hodgkin's disease, acute	1
produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunoomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunoomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein I alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al.,	produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al.,

				approach" Chapter 6:138-160	plasmacytomas, multiple
				(2000); Satthaporn and Eremin,	myeloma, Burkitt's lymphoma,
				J R Coll Surg Ednb 45(1):9-19	arthritis, AIDS, granulomatous
				(2001); Drakes et al., Transp	disease, inflammatory bowel
				Immunol 8(1):17-29 (2000);	disease, sepsis, neutropenia,
				Verhasselt et al., J Immunol	neutrophilia, psoriasis,
				158:2919-2925 (1997); and	suppression of immune
				Nardelli et al., J Leukoc Biol	reactions to transplanted organs
				65:822-828 (1999), the contents	and tissues, hemophilia,
				of each of which are herein	hypercoagulation, diabetes
				incorporated by reference in its	mellitus, endocarditis,
				entirety. Human dendritic cells	meningitis, Lyme Disease,
				that may be used according to	asthma, and allergy.
				these assays may be isolated	Preferred indications also
				using techniques disclosed	include neoplastic diseases (e.g.,
				herein or otherwise known in	leukemia, lymphoma, and/or as
				the art. Human dendritic cells	described below under
				are antigen presenting cells in	"Hyperproliferative Disorders").
				suspension culture, which, when	Highly preferred indications
				activated by antigen and/or	include neoplasms and cancers,
				cytokines, initiate and	such as, leukemia, lymphoma,
				upregulate T cell proliferation	prostate, breast, lung, colon,
				and functional activities.	pancreatic, esophageal, stomach,
					brain, liver, and urinary cancer.
					Other preferred indications
-					include benign dysproliferative
					disorders and pre-neoplastic
	_				conditions, such as, for example,
					hyperplasia, metaplasia, and/or
					dysplasia.
	HDTAU35	505	Production of TNF	TNFa FMAT. Assays for	A highly preferred
91			alpha by dendritic	immunomodulatory proteins	embodiment of the invention

cells	produced by activated	includes a method for inhibiting
	macrophages, T cells,	(e.g., decreasing) TNF alpha
	fibroblasts, smooth muscle, and	production. An alternative
	other cell types that exert a wide	highly preferred embodiment of
	variety of inflammatory and	the invention includes a method
	cytotoxic effects on a variety of	for stimulating (e.g., increasing)
	cells are well known in the art	TNF alpha production.
	and may be used or routinely	Highly preferred indications
	modified to assess the ability of	include blood disorders (e.g., as
	polypeptides of the invention	described below under "Immune
	(including antibodies and	Activity", "Blood-Related
	agonists or antagonists of the	Disorders", and/or
	invention) to mediate	"Cardiovascular Disorders"),
	immunomodulation, modulate	Highly preferred indications
	inflammation and cytotoxicity.	include autoimmune diseases
	Exemplary assays that test for	(e.g., rheumatoid arthritis,
	immunomodulatory proteins	systemic lupus erythematosis,
	evaluate the production of	Crohn"s disease, multiple
	cytokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
	of an inflammatory or cytotoxic	boosting a T cell-mediated
	response. Such assays that may	immune response, and
	be used or routinely modified to	suppressing a T cell-mediated
	test immunomodulatory activity	immune response. Additional
	of polypeptides of the invention	highly preferred indications
	(including antibodies and	include inflammation and
	agonists or antagonists of the	inflammatory disorders, and
	invention) include assays	treating joint damage in patients
	disclosed in Miraglia et al., J	with rheumatoid arthritis. An
	Biomolecular Screening 4:193-	additional highly preferred
	204(1999); Rowland et al.,	indication is sepsis. Highly
	"Lymphocytes: a practical	preferred indications include

neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under	"Hyperproliferative Disorders"). Additionally, highly preferred	indications include neoptasms and cancers, such as, leukemia,	lymphoma, melanoma, glioma (e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,			indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophilia,	psoriasis, suppression of	immune reactions to	transplanted organs and tissues, hemophilia hypercoapulation.
approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890	(1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998);	Vernasseit et al., J Immunol 158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells that may be used according to	these assays may be isolated	using techniques disclosed	herein or otherwise known in	the art. Human dendritic cells	are antigen presenting cells in	suspension culture, which, when	activated by antigen and/or	cytokines, initiate and	upregulate T cell proliferation	and functional activities.									
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HDTAU35				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication is
				infection (e.g., an infectious
	-			disease as described below
				under "Infectious Disease").
16	505	Production of IL-8	Assays measuring production of	Highly preferred indications
		by by endothelial	IL-8 are well known in the art	include immunological and
		cells (such as	and may be used or routinely	inflammatory disorders (e.g.,
		Human Umbilical	modified to assess the ability of	such as allergy, asthma,
		Cord Endothelial	polypeptides of the invention	leukemia, etc. and as described
		Cells).	(including antibodies and	below under "Immune Activity",
			agonists or antagonists of the	and "Blood-Related Disorders").
			invention) to regulate	Highly preferred indications
			production and/or secretion of	also includie autoimmune
			IL-8. For example, FMAT may	disorders (e.g., rheumatoid
			be used or routinely modified to	arthritis, systemic lupus
			assess the ability of	erythematosis, Crohn's disease,
			polypeptides of the invention	multiple sclerosis and/or as
			(including antibodies and	described below), neoplastic
			agonists or antagonists of the	disorders (e.g., organ cancers
			invention) to regulate	such as lung, liver, colon cancer,
			production and/or secretion of	and/or as described below under
			IL-8 from endothelial cells	"Hyperproliferative Disorders"),
			(such as human umbilical vein	and cardiovascular disorders
			endothelial cells (HUVEC)).	(e.g. such as described below
			HUVECs are endothelial cells	under "Cardiovascular
			which line venous blood vessels,	Disorders"). Preferred
			and are involved in functions	indications include thrombosis,
			that include, but are not limited	bacteremia and sepsis syndrome

		to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Endothelial cells play a pivotal role in the initiation and perpetuation of inflammation and secretion of IL-8 may play an important role in recruitment and activation of immune cells such as neutrophils, macrophages, and lymphocytes.	and consequent complications (such as acute respiratory distress syndrome and systemic ischemia-reperfusion resulting from septic shock), restnosis and atherosclerosis.
HDTAU35	 Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-I expresssion in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell	Highly preferred indications include inflammation (acute and chronic), restnosis, athma and allergy. Highly preferred indications include inflammatory disorders, immunological disorders, neoplastic disorders (actiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms and cancers such as, for example, leukemia, lymphoma, and cancers such as, for example, leukemia, lymphoma,

				endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory	and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
92	HDTAV54	506	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),

Highly preferred indications include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under		Additionally, highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other
immunomodulation, modulate inflammation and cytotoxicity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or cytotoxic	response. Such assays that may	be used or routinely modified to	test immunomodulatory activity	of polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J Immunol	160(7):3585-3593 (1998);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells	that may be used according to
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			these assays may be isolated using techniques disclosed	preferred indications include benign dysproliferative
			the art. Human dendritic cells	conditions, such as, for example,
			are antigen presenting cells in	hyperplasia, metaplasia, and/or
			activated by antigen and/or	indications include anemia,
		W- 1	cytokines, initiate and	pancytopenia, leukopenia,
			upregulate T cell proliferation	thrombocytopenia, Hodgkin's
			and functional activities.	disease, acute lymphocytic
				anemia (ALL), plasmacytomas,
				multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
				granulomatous disease,
		,		inflammatory bowel disease,
				neutropenia, neutrophilia,
				psoriasis, suppression of
				immune reactions to
				transplanted organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication is
				infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HDTGW48	507	Activation of	Assays for the activation of	Preferred embodiments of the
		transcription through	transcription through the NFKB	invention include using
		NFKB response	response element are well-	polypeptides of the invention (or
		element in immune	known in the art and may be	antibodies, agonists, or

antagonists thereof) in detection,	diagnosis, prevention, and/or	treatment of Cancer,	Autoimmunity, Allergy and	Asthma																												
used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the NFKB	response element that may be	used or rountinely modified to	test NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Gri G, et al., Biol	Chem, 273(11):6431-6438	(1998); Pyatt DW, et al., Cell	Biol Toxicol 2000;16(1):41-51	(2000); Berger et al., Gene 66:1-	10 (1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844
cells (such as B-	cells).																															
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				(1999), the contents of each of which are herein incorporated by reference in its entirety.	
				Immune cells that may be used according to these assays are	
				publicly available (e.g., through	
				cells that may be used according	
				to these assays include the Reh	
	HDTI M18	508	Production of	MIP-Talpha FMAT Assays for	A highly preferred
94)	MIPlalpha	immunomodulatory proteins	embodiment of the invention
			•	produced by activated dendritic	includes a method for
				cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well known	embodiment of the invention
				in the art and may be used or	includes a method for inhibiting
				routinely modified to assess the	(e.g., reducing) MIP1a
				ability of polypeptides of the	production. A highly
				invention (including antibodies	preferred indication is infection
				and agonists or antagonists of	(e.g., an infectious disease as
				the invention) to mediate	described below under
				immunomodulation, modulate	"Infectious Disease").
				chemotaxis, and modulate T cell	Preferred indications include
				differentiation. Exemplary	blood disorders (e.g., as
				assays that test for	described below under "Immune
				immunomodulatory proteins	Activity", "Blood-Related
	-			evaluate the production of	Disorders", and/or
				chemokines, such as	"Cardiovascular Disorders").
				macrophage inflammatory	Highly preferred indications
				protein 1 alpha (MIP-1a), and	include autoimmune diseases
				the activation of	(e.g., rheumatoid arthritis,

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systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional	highly preferred indications include inflammation and	inflammatory disorders. Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lympnocytic anemia (ALL), plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Highly preferred indications
monocytes/macrophages and T cells. Such assays that may be used or routinely modified to	test immunomodulatory and chemotaxis activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical annroach" Chapter 6:138-160	(2000); Satthaporn and Eremin,	J R Coll Surg Ednb 45(1):9-19	(2001); Drakes et al., Transp	Immunol 8(1):17-29 (2000);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells	that may be used according to	these assays may be isolated	using techniques disclosed	herein or otherwise known in	the art. Human dendritic cells	are antigen presenting cells in	suspension culture, which, when
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such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.
cytokines, initiate and upregulate T cell proliferation and functional activities.	Assays for production of IL-13 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-13 and/or activation of T-cells. Exemplary assays for IL-13 production that may be used or routinely modified to test activity of polypeptides and antibodies of the invention (including agonists or antagonists of such invention) include, for example, assays such as disclosed and/or cited in: Grunig, G, et al., "Requirement for IL-13
	Production of IL-13 and activation of T-cells.
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	HDTLM18
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	Preferred embodiments of the invention include using polypeptides of the invention (or
independently of IL-4 in Experimental asthma" Science;282: 2261-2263 (1998), and Wills-Karp M, et al., "Interleukin-13: central mediator of allergic asthma" Science; 282: 2258-2261 (1998); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL13, a Th2 type cytokine, is a potent stimulus for mucus production, airway hyper-responsiveness and allergic asthma. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and asthma. Primary T helper 2 cells are generated in in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes	isolated from cord blood. Assays for the activation of transcription through the Gamma Interferon Activation
	Activation of transcription through GAS response
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element in epithelial	Site (GAS) response element are	antibodies, agonists, or
 cells (such as HELA	well-known in the art and may	antagonists thereof) in detection,
 cells).	be used or routinely modified to	diagnosis, prevention, and/or
	assess the ability of	treatment of Cancer, Wound
	polypeptides of the invention	Healing, and Inflamation.
	(including antibodies and	Highly preferred indications
	agonists or antagonists of the	include neoplastic diseases (e.g.,
 	invention) to regulate STAT	as described below under
-	transcription factors and	"Hyperproliferative Disorders").
	modulate gene expression	Highly preferred indications
	involved in a wide variety of	include neoplasms and cancers,
	cell functions. Exemplary	such as, for example, melanoma,
	assays for transcription through	and prostate, breast, lung, colon,
	the GAS response element that	pancreatic, esophageal, stomach,
	may be used or routinely	brain, liver and urinary cancer.
,	modified to test GAS-response	Other preferred indications
	element activity of polypeptides	include benign dysproliferative
	of the invention (including	disorders and pre-neoplastic
<u> </u>	antibodies and agonists or	conditions, such as, for example,
	antagonists of the invention)	'n,
	include assays disclosed in:	dysplasia. Preferred
	You M, et al, J Biol Chem,	indications include include
	272(37):23376-23381(1997);	inflammation and inflammatory
	Min W, et al., Circ Res,	disorders.
	83(8):815-823 (1998); Berger et	
	al., Gene 66:1-10 (1998); Cullen	
	and Malm, Methods in Enzymol	
	216:362-368 (1992); Henthorn	
	et al., Proc Natl Acad Sci USA	
	85:6342-6346 (1988);	
	Matikainen et al., Blood	
	93(6):1980-1991 (1999); and	
	Henttinen et al., J Immunol	

	disclosed in Forrer et al Biol	the invention includes a method
	Chem 379(8-9)·1101-1110	for inhihiting adinocyte
	(1998): Nikoulina et al	differentiation. Highly
	 Diabetes 49(2):263-271 (2000);	≘
	and Schreyer et al., Diabetes	endocrine disorders (e.g., as
	48(8):1662-1666 (1999), the	described below under
	contents of each of which are	"Endocrine Disorders").
	herein incorporated by reference	Preferred indications include
	in its entirety. Mouse adipocyte	neoplastic diseases (e.g.,
	cells that may be used according	lipomas, liposarcomas, and/or as
	to these assays are publicly	described below under
	available (e.g., through the	"Hyperproliferative Disorders"),
	ATCC). Exemplary mouse	blood disorders (e.g.,
	adipocyte cells that may be used	hypertension, congestive heart
 	according to these assays	failure, blood vessel blockage,
	include 3T3-L1 cells. 3T3-L1 is	heart disease, stroke, impotence
	an adherent mouse preadipocyte	and/or as described below under
	cell line that is a continous	"Immune Activity",
	substrain of 3T3 fibroblast cells	"Cardiovascular Disorders",
	developed through clonal	and/or "Blood-Related
	isolation and undergo a pre-	Disorders"), immune disorders
	adipocyte to adipose-like	(e.g., as described below under
	 conversion under appropriate	"Immune Activity"), neural
	differentiation conditions known	disorders (e.g., as described
	in the art.	below under "Neural Activity
		and Neurological Diseases"),
		and infection (e.g., as described
		below under "Infectious
		Disease"). A highly
		preferred indication is diabetes
		mellitus. An additional
		highly preferred indication is a
		complication associated with

infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract	and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity.	ingling properties include very, weight highly properties are composite with insurance in the composite in t	highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disorded described described and highly preferred indications include, hypertension, coronary artery disorded described de	gallstones, osteoarthritis, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma,
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reast, I ma, I, Other de c c mple, d/or	tt of ethod gg) nn nn ne mune mune ms ses
lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for Stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
lymphoma, leukemia and colon, and kidney cancer. Additional highly preferre indications include melan prostate, lung, pancreati, esophageal, stomach, bra liver, and urinary cancer. preferred indications inclubenign dysproliferative disorders and pre-neoplas conditions, such as, for ey hyperplasia, metaplasia, a dysplasia.	A preferred embodim the invention includes a for inhibiting (e.g., redu TNF alpha production. / alternative preferred embodiment of the invenincludes a method for stimulating (e.g., increastimulating (e.g., increastimulating (e.g., increastimulating), "Blood-Relat Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disorder Highly preferred indicat include autoimmune dis (e.g., rheumatoid arthrit systemic lupus erythems
lymphome colon, and Additiona indication prostate, lesophagea liver, and preferred i benign dy disorders conditions hyperplasia	A p the inv for inh TNF al alterna embod include stimule TNF al Preferr blood c describ Activit Activit Highly include (e.g., r system
	of serum) are d may lifred to lifred to ntion d f the e serum dulate involved ssays the t t SRE t SRE
	activation rough the ent (SRE ent (SRE ent (SRE ent an inely mochinely mochinely mochinely and genists of genes and mochinely a nuthrough or used on through or used on collypeptical agonists agonists
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or
	of n through onse mmune as T-
	Activation of transcription through serum response element in immune cells (such as T-cells).
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Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and sumressing a T cell-mediated	immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly	preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic
antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci 118A	85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the	ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.

					conditions, such as, for example,
					hynernlasia metanlasia and/or
					dysplasia. Preferred
					indications include anemia,
					pancytopenia, leukopenia,
					thrombocytopenia, Hodgkin's
					disease, acute lymphocytic
					anemia (ALL), plasmacytomas,
					multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					neutropenia, neutrophilia,
					psoriasis, suppression of
					immune reactions to
					transplanted organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
-					additional preferred indication is
					infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HE6AU52	511	Activation of	Assays for the activation of	Preferred indications include
26			transcription through	transcription through the cAMP	blood disorders (e.g., as
			cAMP response	response element are well-	described below under "Immune
			element in immune	known in the art and may be	Activity", "Blood-Related
			cells (such as T-	used or routinely modified to	Disorders", and/or
			cells).	assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an infectious

				to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and
97	HE6AU52	511	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and	asthma and allergy. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly

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preferred indications include blood disorders (e.g., as described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as described	Disease"). Highly preferred	indications include autoimmune	diseases (e.g., rheumatoid	arthritis, systemic lupus	erythematosis, multiple sclerosis	and/or as described below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response and	alternatively suppressing a B	cell-mediated immune response.	Highly preferred indications	include inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative
chronic hyperproliferative diseases. Assays for immunomodulatory and	differentiation factor proteins	produced by a large variety of	cells where the expression level	is strongly regulated by	hormones are well known in the	art and may be used or routinely	modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and the	stimulation and upregulation of	T cell proliferation and	functional activities. Such	assays that may be used or	routinely modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays
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Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.	An additonal preferred	indication is infection (e.g., an	hafiantions disease as described
disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which, when	activated by antigen and/or	cytokines, initiate and	upregulate T cell proliferation	and functional activities.						49					
																														•••		
															-																	

					below under "Infectious
					Disease").
	HE6AU52	511	Production of TNF	TNFa FMAT. Assays for	A highly preferred
97			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for inhibiting
				macrophages, T cells,	(e.g., decreasing) TNF alpha
				fibroblasts, smooth muscle, and	production. An alternative
				other cell types that exert a wide	highly preferred embodiment of
				variety of inflammatory and	the invention includes a method
				cytotoxic effects on a variety of	for stimulating (e.g., increasing)
				cells are well known in the art	TNF alpha production.
				and may be used or routinely	Highly preferred indications
				modified to assess the ability of	include blood disorders (e.g., as
			-	polypeptides of the invention	described below under "Immune
				(including antibodies and	Activity", "Blood-Related
				agonists or antagonists of the	Disorders", and/or
				invention) to mediate	"Cardiovascular Disorders"),
				immunomodulation, modulate	Highly preferred indications
				inflammation and cytotoxicity.	include autoimmune diseases
				Exemplary assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn's disease, multiple
-				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
				and the induction or inhibition	(e.g., as described below),
				of an inflammatory or cytotoxic	boosting a T cell-mediated
				response. Such assays that may	immune response, and
				be used or routinely modified to	suppressing a T cell-mediated
				test immunomodulatory activity	immune response. Additional
				of polypeptides of the invention	highly preferred indications
				(including antibodies and	include inflammation and
				agonists or antagonists of the	inflammatory disorders, and

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treating joint damage in patients with rheumatoid arthritis. An	additional highly preferred	indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,
invention) include assays	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J Immunol	160(7):3585-3593 (1998);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells	that may be used according to	these assays may be isolated	using techniques disclosed	herein or otherwise known in	the art. Human dendritic cells	are antigen presenting cells in	suspension culture, which, when	activated by antigen and/or	cytokines, initiate and	upregulate T cell proliferation	and functional activities.					
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neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A nignly preserved embodument of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and
	Production of IL-6
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	HE6CS65
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hormones are well known in the	Disease"). Highly preferred
art and may be used or routinely	indications include autoimmune
modified to assess the ability of	diseases (e.g., rheumatoid
polypeptides of the invention	arthritis, systemic lupus
(including antibodies and	erythematosis, multiple sclerosis
agonists or antagonists of the	and/or as described below) and
invention) to mediate	immunodeficiencies (e.g., as
immunomodulation and	described below). Highly
differentiation and modulate T	preferred indications also
cell proliferation and function.	include boosting a B cell-
Exemplary assays that test for	mediated immune response and
immunomodulatory proteins	alternatively suppressing a B
evaluate the production of	cell-mediated immune response.
cytokines, such as IL-6, and the	Highly preferred indications
stimulation and upregulation of	include inflammation and
T cell proliferation and	inflammatory
functional activities. Such	disorders.Additional highly
assays that may be used or	preferred indications include
routinely modified to test	asthma and allergy. Highly
immunomodulatory and	preferred indications include
diffferentiation activity of	neoplastic diseases (e.g.,
polypeptides of the invention	myeloma, plasmacytoma,
(including antibodies and	leukemia, lymphoma,
 agonists or antagonists of the	melanoma, and/or as described
invention) include assays	below under "Hyperproliferative
disclosed in Miraglia et al., J	Disorders"). Highly preferred
 Biomolecular Screening 4:193-	indications include neoplasms
204(1999); Rowland et al.,	and cancers, such as, myeloma,
"Lymphocytes: a practical	plasmacytoma, leukemia,
approach" Chapter 6:138-160	lymphoma, melanoma, and
 (2000); and Verhasselt et al., J	prostate, breast, lung, colon,
Immunol 158:2919-2925	pancreatic, esophageal, stomach,
 (1997), the contents of each of	brain, liver and urinary cancer.

Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An
which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of
	Production of MCP-1
	512
	HE6CS65
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				(2001): and Verhasselt et al I	lymphoma, arthritis, AIDS,
				Immunol 158:2919-2925	granulomatous disease,
				(1997), the contents of each of	inflammatory bowel disease,
-				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Human dendritic cells that may	suppression of immune
		_		be used according to these	reactions to transplanted organs
				assays may be isolated using	and tissues, hemophilia,
		-		techniques disclosed herein or	hypercoagulation, diabetes
				otherwise known in the art.	mellitus, endocarditis,
				Human dendritic cells are	meningitis (bacterial and viral),
				antigen presenting cells in	Lyme Disease, asthma, and
		•		suspension culture, which, when	allergy Preferred indications
				activated by antigen and/or	also include neoplastic diseases
				cytokines, initiate and	(e.g., leukemia, lymphoma,
				unregulate T cell proliferation	and/or as described below under
				and functional activities.	"Hyperproliferative Disorders").
					Highly preferred indications
					include neoplasms and cancers,
					such as, leukemia, lymphoma,
					prostate, breast, lung, colon,
					pancreatic, esophageal, stomach,
					brain, liver, and urinary cancer.
					Other preferred indications
					include benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for example,
					hyperplasia, metaplasia, and/or
		-			dysplasia.
	HE6CS65	512	Production of IL-10	Assays for production of IL-10	Highly preferred indications
86			and activation of T-	and activation of T-cells are	include allergy and astrima.
			cells.	well known in the art and may	Additional highly preferred

	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders").
Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as
	Production of MIP1alpha
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Highly preferred indications	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	Land holow under
macrophage inflammatory	protein 1 alpha (Mir - 1a), and the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and Eremin,	J R Coll Surg Ednb 45(1):9-19	(2001); Drakes et al., Transp	Immunol 8(1):17-29 (2000);	Verhasselt et al., J Immunol	158:2919-2925 (1997); and	Nardelli et al., J Leukoc Biol	65:822-828 (1999), the contents	of each of which are herein	incorporated by reference in its	entirety. Human dendritic cells	that may be used according to	these assays may be isolated	using techniques disclosed	herein or otherwise known in	
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"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic
are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely
	Activation of transcription through GAS response element in immune cells (such as Teells).
·	514
	HE6EY13
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element activity of polypeptides conditions, such as, for example, of the invention (including antibodies and agonists or antibodies and agonists or be invention) include assays disclosed in Eastward antipulation antipulation antipulation of the invention include assays disclosed in Eastward Malin. (1988). Culler and Malin. Methods in Enzymol 216:362- Berger et al., Gene 66:10 368 (1992). Henthom et al., proved below), prosting a T Eell-more et al., prove 141 Acad Sci USA 85:5342-6346 (1988); and suppressing a T Cell-mediated immune response. Hentinen et al., Ill munuol below, boosting a T Cell-mediated immune response. Additional preferred indications include nemanation and suppressing a T Cell-mediated immune response. Additional preferred indications in its entirety. Exemplary herein incorporated by reference according to these assays are cell-mediated below under "Immune SULP T cell, inc, that may be used Activity.", "Blood-Related according to these assays are Disorders", and/or an infection sascoited with chronic granulomatosus disease and malignant osteoporosis, and/or an infection sascoited with chronic granulomatosus disease and malignant osteoporosis, and/or an infection sascoited with chronic granulomatosus disease and malignant osteoporosis, and/or an infection sascoited with chronic granulomatosus disease and malignant osteoporosis, and/or an infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infections include additional preferred indications include indications include indications include before indications include																																	\neg
element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:634-6346 (1988); Marikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995); the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	Conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune response,	and suppressing a T cell-	mediated immune response.	Additional preferred indications	include inflammation and	inflammatory disorders. Highly			described below under "Immune			"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus disease	and malignant osteoporosis,	and/or an infectious disease as	described below under	"Infectious Disease"). An	additional preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include
	1 -1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by reference	in its entirety. Exemplary	human T cells, such as the	SUPT cell line, that may be used	according to these assays are	publicly available (e.g., through	the ATCC).	`									
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anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Diabetes A highly preferred indication is diabetes. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve diabetic neuropathy, hood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy), blood vessel stroke, impotence (e.g., due to diabetic neuropathy or
	Kinase assay: measures the phosphorylation of Elk-1, an indication of activation of extracellular signal regulated kinase (ERK). ERK pathway regulates cell growth, proliferation and differentiation. Cells were pretreated with SID supernatants for 15-18 hours, and then 100 nM of insulin was added to stimulate ERK kinase. Phosphorylation of Elk-1 was measured after a 20 minute incubation. Pre-adipocytes that may be used according to these assays are publicly available
·	Inhibition of adipocyte ERK signaling pathway.
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blood vessel blockage), seizures,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g., heart	disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and outer	diseases allu disolucis as	described in the Cardiovascular Disorders' section below)	dyslinidemia endocrine disorders	(as described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the urinary	tract and skin). Highly preferred	indications also include obesity,	weight gain, and weight loss, as	well as complications associated	with obesity, weight gain, and	weight loss. Preferred	embodiments of the invention	include methods of preventing,	detecting, diagnosing, treating	and/or ameliorating the above	mentioned conditions, disorders,	and diseases.
(e.g., through the ATCC) and/or	may be routinely generated. Exemplary mouse adipocyte	cells that may be used according	to these assays include 3T3-L1	cells. 3T3-L1 is an adherent	mouse preadipocyte cell line	that is a continuous substrain of	3T3 fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.	Cells were differentiated to an	adipose-like state before being	used in the screen. See Green et	al., Cell 3: 127-133 (1974), the	contents of which are herein	incorporated by reference in its	entirety.												
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Highly preferred indications include asthma, allergy, hypersensitivity reactions,	inflammation, and inflammatory disorders. Additional highly	preferred indications include	disorders (e.g., as described	below under "Immune Activity",	and "Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting or inhibiting	immune cell proliferation.	Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Highly preferred indications	include boosting an eosinophil-	mediated immune response, and	suppressing an eosinophil-	mediated immune response.			
Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation,	activation, or apoptosis are well known in the art and may be	used or routinely modified to	assess the ability of polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to promote or inhibit	cell proliferation, activation, and	apoptosis. Exemplary assays for	JNK kinase activity that may be	used or routinely modified to	test JNK kinase-induced activity	of polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Gupta et al., Exp Cell	Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.
Activation of JNK Signaling Pathway in immune cells	(such as eosinophils).																											
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Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in the	late stage of allergic reactions;	they are recruited to tissues and	mediate the inflammatory	response of late stage allergic	reaction. Moreover, exemplary	assays that may be used or	routinely modified to assess the	ability of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils include	assays disclosed and/or cited in:	Zhang JP, et al., "Role of	caspases in dexamethasone-	induced apoptosis and activation	of c-Jun NH2-terminal kinase	and p38 mitogen-activated	protein kinase in human	eosinophils" Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al., "Disruption	of fas receptor signaling by	nitric oxide in eosinophils" J	Exp Med; Feb 2;187(3):415-25	(1998); J Allergy Clin Immunol	1999 Sep;104(3 Pt 1):565-74;
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	Immune Highly preferred indications include immunological disorders such as described herein under the heading "Immune Activity" and/or "Blood-Related Disorders" (particularly including, but not limited to, immune disorders involving endothelial cells). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating disorders of the immune system (particularly including, but not limited to, immune disorders involving endothelial cells). (HUVEC cells are human umbilical vein endothelial cells).
and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the immunomodulation, induce chemotaxis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells.
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
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Such assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC). Exemplary	endothelial cells that may be	used according to these assays	include human umbilical vein	endothelial cells (HUVEC),	which are endothelial cells	which line venous blood vessels,	and are involved in functions	that include, but are not limited	to, angiogenesis, vascular	permeability, vascular tone, and
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				immune cell extravasation.	
	HE8BQ49	515	Production of	Assays for measuring	Highly preferred indications
101	, 		VCAM in	expression of VCAM are well-	include inflammation (acute and
			endothelial cells	known in the art and may be	chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and inflammatory
			<u>, </u>	agonists or antagonists of the	disorders, immunological
				invention) to regulate VCAM	disorders, neoplastic disorders
	•			expression. For example,	(e.g. cancer/tumorigenesis), and
				FMAT may be used to meaure	cardiovascular disorders (such
				the upregulation of cell surface	as described below under
				VCAM-I expresssion in	"Immune Activity", "Blood-
			-	endothelial cells. Endothelial	Related Disorders",
				cells are cells that line blood	"Hyperproliferative Disorders"
				vessels, and are involved in	and/or "Cardiovascular
				functions that include, but are	Disorders"). Highly preferred
				not limited to, angiogenesis,	indications include neoplasms
				vascular permeability, vascular	and cancers such as, for
				tone, and immune cell	example, leukemia, lymphoma,
				extravasation. Exemplary	melanoma, renal cell carcinoma,
		_		endothelial cells that may be	and prostate, breast, lung, colon,
				used according to these assays	pancreatic, esophageal, stomach,
				include human umbilical vein	brain, liver and urinary cancer.
				endothelial cells (HUVEC),	Other preferred indications
_				which are available from	include benign dysproliferative
				commercial sources. The	disorders and pre-neoplastic
				expression of VCAM (CD106),	conditions, such as, for example,
				a membrane-associated protein,	hyperplasia, metaplasia, and/or
				can be upregulated by cytokines	dysplasia.
				or other factors, and contributes	

		Preferred embodiments of the
to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours. LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its	Assays for measuring
	Activation of Transcription	Production of
	515	516
	HE8BQ49	HE8SG96
	101	

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invention include using not properties of the invention (or	antibodies, agonists, or	antagonists thereof) in detection,	diagnosis, prevention, and/or	treatment of Vascular Disease,	Atherosclerosis, Restenosis,	Stroke, and Asthma.																								A highly preferred
expression of ICAM-1 are well-	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate ICAM-1	expression. Exemplary assays	that may be used or routinely	modified to measure ICAM-1	expression include assays	disclosed in: Rolfe BE, et al.,	Atherosclerosis, 149(1):99-110	(2000); Panettieri RA Jr, et al., J	Immunol, 154(5):2358-2365	(1995); and, Grunstein MM, et	al., Am J Physiol Lung Cell Mol	Physiol, 278(6):L1154-L1163	(2000), the contents of each of	which is herein incorporated by	reference in its entirety. Cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be routinely	generated. Exemplary cells that	may be used according to these	assays include Aortic Smooth	Muscle Cells (AOSMC); such	as bovine AOSMC.	Assays for the activation of
ICAM-1																					-									Activation of
																														517
																														HE9CY05
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indication includes allergy. A highly preferred indication includes asthma. A highly preferred indication includes rhinitis. Additional highly	preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders.	indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").	Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described	
transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of genes	important for Th2 immune response development. Exemplary assays for transcription through the GATA3 response element that may be used or routinely	modified to test GATA3- response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924
transcription through GATA-3 response element in immune cells (such as Teells).				,
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				(1999); Zheng and Flavell, Cell	melanoma, and prostate, breast,
				89(4):587-596 (1997); and Henderson et al Mol Cell Biol	lung, colon, pancreatic,
				14(6):4286-4294 (1994), the	liver and urinary cancer. Other
				contents of each of which are	preferred indications include
				herein incorporated by reference	benign dysproliferative
				in its entirety. T cells that may	disorders and pre-neoplastic
				be used according to these	conditions, such as, for example,
				assays are publicly available	hyperplasia, metaplasia, and/or
				(e.g., through the ATCC).	dysplasia. Preferred
				Exemplary mouse T cells that	indications include anemia,
				may be used according to these	pancytopenia, leukopenia,
				assays include the HT2 cell line,	thrombocytopenia, leukemias,
				which is a suspension culture of	Hodgkin's disease, acute
				IL-2 dependent T cells that also	lymphocytic anemia (ALL),
				respond to IL-4.	plasmacytomas, multiple
				•	myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted organs
	-				and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, and Lyme Disease.
	HE9GG20	518	Production of	Assays for measuring	Preferred embodiments of the
104			ICAM-1	expression of ICAM-1 are well-	invention include using
				known in the art and may be	polypeptides of the invention (or
				used or routinely modified to	antibodies, agonists, or
				assess the ability of	antagonists thereof) in detection,
					-

			polypeptides of the invention (including antibodies and	diagnosis, prevention, and/or treatment of Inflammation,
			agonists or antagonists of the invention) to regulate ICAM-1	Vascular Disease, Athereosclerosis, Restenosis,
			expression. Exemplary assays	and Stroke
			that may be used or routinely	
			modified to measure ICAM-1	
			expression include assays	
			disclosed in: Takacs P, et al,	
			FASEB J, 15(2):279-281	
			(2001); and, Miyamoto K, et al.,	
			Am J Pathol, 156(5):1733-1739	
			(2000), the contents of each of	
			which is herein incorporated by	
			reference in its entirety. Cells	
			that may be used according to	
			these assays are publicly	
			available (e.g., through the	
			ATCC) and/or may be routinely	
			generated. Exemplary cells that	
-			may be used according to these	
			assays include microvascular	
			endothelial cells (MVEC).	
HEAAW94	519	Production of IL-10	Assays for production of IL-10	Highly preferred indications
		and activation of T-	and activation of T-cells are	include allergy and asthma.
		cells.	well known in the art and may	Additional highly preferred
			be used or routinely modified to	indications include immune and
			assess the ability of	hematopoietic disorders (e.g., as
			polypeptides of the invention	described below under "Immune
			(including antibodies and	Activity", and "Blood-Related
			agonists or antagonists of the	Disorders"), autoimmune
			invention) to stimulate or inhibit	diseases (e.g., rheumatoid

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			artinitis, systemic lupus
	ac	activation of 1-cells.	erythematosis, Crohn's disease,
	EX	Exemplary assays that may be	multiple sclerosis and/or as
	sn	used or routinely modified to	described below),
	SE	assess the ability of	immunodeficiencies (e.g., as
	00	polynentides and antibodies of	described below), boosting a T
	24. 14.	the invention (including agonists	cell-mediated immine response
		or antagonists of the invention)	and cumpressing a T cell-
		antagomists of the myention)	and suppressing a 1 cent
	to	to modulate IL-10 production	mediated immune response.
	an	and/or T-cell proliferation	
	inc	include, for example, assays	
	ns	such as disclosed and/or cited	
	iui —	in: Robinson, DS, et al., "Th-2	
	ck	cytokines in allergic disease" Br	
	Ņ	Med Bull; 56 (4): 956-968	
		(2000), and Cohn, et al., "T-	
	he	helper type 2 cell-directed	
	the	therapy for asthma"	
	Ph Bh	Pharmacology & Therapeutics;	
	88	88: 187-196 (2000); the contents	
	do of	of each of which are herein	
	oui	incorporated by reference in	
-	the	their entirety. Exemplary cells	
	the	that may be used according to	
	the	these assays include Th2 cells.	
	11	IL10 secreted from Th2 cells	
	<u> </u>	may be measured as a marker of	
		Th2 cell activation. Th2 cells	
	are	are a class of T cells that secrete	
	<u> </u>	IL4, IL10, IL13, IL5 and IL6.	
-	Fa	Factors that induce	
-	lib	differentiation and activation of	
	T	Th2 cells play a major role in	

	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred inflammation and inflammatory disorders. An additional highly preferred inflammation is infection (e.g., an infectious disease as described below under
the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene
	Activation of transcription through NFAT response element in immune cells (such as Teells).
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Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as	described below under "Hyperproliferative Disorders"). Preferred indications include	neoplasms and cancers, such as, for example, leukemia,	lympholina, and prostate, organi, lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications also include anemia,	pancytopenia, leukopenia,	thrombocytopenia, riodgkiii s disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et	al., Int J Biochem Cell Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Veseen et al. I Biol Chem	268(19):14285-14293 (1993), the contents of each of which	are herein incorporated by	reference in its entirety. T cells	that may be used according to these assays are publicly	available (e.g., through the	ATCC). Exemplary human T	cells that may be used according	to these assays include the	suspension culture of IL-2 and	IL-4 responsive T cells.					-				
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					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HEBDF77	521	Activation of	Assays for the activation of	A preferred embodiment of
107	· · · · · · · · · · · · · · · · · · ·		transcription through	transcription through the Serum	the invention includes a method
			serum response	Response Element (SRE) are	for inhibiting (e.g., reducing)
			element in immune	well-known in the art and may	TNF alpha production. An
			cells (such as T-	be used or routinely modified to	alternative preferred
			cells).	assess the ability of	embodiment of the invention
				polypeptides of the invention	includes a method for
				(including antibodies and	stimulating (e.g., increasing)
				agonists or antagonists of the	TNF alpha production.
			`	invention) to regulate the serum	Preferred indications include
_			_	response factors and modulate	blood disorders (e.g., as
				the expression of genes involved	described below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
_				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated
				85:6342-6346 (1988); and Black	immune response. Additional
				et al., Virus Genes 12(2):105-	highly preferred indications
				117 (1997), the content of each	include inflammation and

inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly	preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as	"Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms	example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid	lung, colon, pancreatic, oreas, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred	indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the	ATCC). Exemplary mouse T cells that may be used according to these assays include the	dependent suspension culture of T cells with cytotoxic activity.		·		

granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Cancer Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders.
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its
	SEAP in HepG2/Squale- synthetase(stimulati on)
	521
	HEBDF77
	107

HEBDF77 52	Activation of		entirety. Assays for activation of	Cancer
			transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours. LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its entirety.	Highly preferred indications include neoplastic diseases (e.g. cancer) such as described herein under the heading "Hyperproliferative Disorders" (particularly including, but not limited to, cancer involving cells of the gastrointestinal tract, particularly the colon). Highly preferred embodiments of the invention include methods of preventing, detecting, diagnosing, treating and/or ameliorating cancer and hyperproliferative disorders involving the gastrointestinal tract, particularly the colon.
неврд91	Activation of transcription transcription cAMP respone element (CRE pre-adipocyte	through se ?) in s.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain.

	eferred	tion	s (e.g.,	betic	sease	ropathy	Þ	n the	on	athy,	damage		el	stroke,	diabetic	ssel	ntal	•	ic-		(e.g.,	erosis,		nd other	1S	ovascular	w),	0)	in the	section	sion	tic
indication is diabetes meillius.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure, nephropathy	and/or other diseases and	disorders as described in the	"Renal Disorders" section	below), diabetic neuropathy,	nerve disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular	Disorders" section below),	dyslipidemia, endocrine	disorders (as described in the	"Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic
	An	indi	asso	diab	nep	(e.g	and/	diso	Re	pelc	ner	(e.g	nen) Ploc	imp	nen	ploc	con	non	hyp	carc	hea	mic	hyp	dise	des	Dis	dys	disc			imr
(including antibodies and	agonists or antagonists of the	invention) to increase cAMP,	regulate CREB transcription	factors, and modulate	expression of genes involved in	a wide variety of cell functions.	For example, a 3T3-L1/CRE	reporter assay may be used to	identify factors that activate the	cAMP signaling pathway.	CREB plays a major role in	adipogenesis, and is involved in	differentiation into adipocytes.	CRE contains the binding	sequence for the transcription	factor CREB (CRE binding	protein). Exemplary assays for	transcription through the cAMP	response element that may be	used or routinely modified to	test cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch et	al Mol Cell Biol 20(3):1008-
<u> </u>																							<u>.</u>									
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(1998), the con which are herei by reference in adjoocytes that according to the publicly available the ATCC) and routinely gener mouse adjoocyte continuous sub fibroblast cells through clonal undergo a pre-adjoocyte continuous sub fibroblast cells through clonal undergo a pre-adjoocytike conditions known transcription through transcription the serum response element in immune well-known in cells (such as T-assess the ability of the conditions and (including antility).	J Biol Chem 273:917-923	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	(1998), the contents of each of which are herein incorporated	healing, and infection (e.g., infectious diseases and disorders
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Teclls).	by reference in its entirety. Pre-	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Teclls).	adipocytes that may be used	Diseases" section below,
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Technolis).	according to these assays are	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Technolis).	publicly available (e.g., through	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Teells).	the ATCC) and/or may be	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Teells).	routinely generated. Exemplary	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	mouse adipocyte cells that may	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	be used according to these	complications associated with
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	assays include 3T3-L1 cells.	insulin resistance.
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Technology).	3T3-L1 is an adherent mouse	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	preadipocyte cell line that is a	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	continuous substrain of 3T3	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Teclls).	fibroblast cells developed	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Teells).	through clonal isolation and	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	undergo a pre-adipocyte to	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Teells).	adipose-like conversion under	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	appropriate differentiation	
HEBDQ91 522 Activation of transcription through serum response element in immune cells (such as Tells).	conditions known in the art.	
transcription through serum response element in immune cells (such as Teells).		A preferred embodiment of
serum response element in immune cells (such as T- cells).	transcription through transcription through the Serum	
eu		for inhibiting (e.g., reducing)
	element in immune well-known in the art and may	
		to alternative preferred
polypeptides of (including antil		embodiment of the invention
(including antil	polypeptides of the invention	includes a method for
\$ 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	(including antibodies and	stimulating (e.g., increasing)
agoinsts of anti-	agonists or antagonists of the	TNF alpha production.
invention) to re	invention) to regulate the serum	n Preferred indications include

		response factors and modulate the expression of genes involved	blood disorders (e.g., as described below under "Immune
		in growth. Exemplary assays	Activity", "Blood-Related
		for transcription through the	Disorders", and/or
		SRE that may be used or	"Cardiovascular Disorders"),
		routinely modified to test SRE	Highly preferred indications
		activity of the polypeptides of	include autoimmune diseases
		the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
		antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and Black	immune response. Additional
-		et al., Virus Genes 12(2):105-	highly preferred indications
		117 (1997), the content of each	include inflammation and
		of which are herein incorporated	inflammatory disorders, and
		by reference in its entirety. T	treating joint damage in patients
		cells that may be used according	with rheumatoid arthritis. An
	•	to these assays are publicly	additional highly preferred
		available (e.g., through the	indication is sepsis. Highly
		ATCC). Exemplary mouse T	preferred indications include
		cells that may be used according	neoplastic diseases (e.g.,
		to these assays include the	leukemia, lymphoma, and/or as
		CTLL cell line, which is an IL-2	described below under
		dependent suspension culture of	"Hyperproliferative Disorders").
		T cells with cytotoxic activity.	Additionally, highly preferred
			indications include neoplasms
			and cancers, such as, for
			example, leukemia, lymphoma,

melanoma, glioma (e.g.,	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophilia,	psoriasis, suppression of	immune reactions to	transplanted organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication is	infection (e.g., an infectious	disease as described below
	-																													

					under "Infectious Disease").
	НЕВDQ91	522	Activation of	This reporter assay measures	Highly preferred indications
108	,		transcription through	activation of the GATA-3	include allergy, asthma, and
			GATA-3 response	signaling pathway in HMC-1	rhinitis. Additional preferred
			element in immune	human mast cell line. Activation	indications include infection
			cells (such as mast	of GATA-3 in mast cells has	(e.g., an infectious disease as
			cells).	been linked to cytokine and	described below under
				chemokine production. Assays	"Infectious Disease"), and
				for the activation of	inflammation and inflammatory
				transcription through the	disorders. Preferred indications
				GATA3 response element are	also include blood disorders
				well-known in the art and may	(e.g., as described below under
				be used or routinely modified to	"Immune Activity", "Blood-
				assess the ability of	Related Disorders", and/or
				polypeptides of the invention	"Cardiovascular Disorders").
				(including antibodies and	Preferred indications include
				agonists or antagonists of the	autoimmune diseases (e.g.,
				invention) to regulate GATA3	rheumatoid arthritis, systemic
				transcription factors and	lupus erythematosis, multiple
				modulate expression of mast	sclerosis and/or as described
				cell genes important for immune	below) and immunodeficiencies
				response development.	(e.g., as described below).
				Exemplary assays for	Preferred indications include
				transcription through the	neoplastic diseases (e.g.,
				GATA3 response element that	leukemia, lymphoma,
				may be used or routinely	melanoma, prostate, breast,
				modified to test GATA3-	lung, colon, pancreatic,
				response element activity of	esophageal, stomach, brain,
				polypeptides of the invention	liver, and urinary tract cancers
				(including antibodies and	and/or as described below under
				agonists or antagonists of the	"Hyperproliferative Disorders").
			and the second s	invention) include assays	Other preferred indications

				disclosed in Berger et al Gene	include benign dysproliferative
-				66.1-10 (1998). Cullen and	disorders and pre-peoplastic
				10(179), Cuncil and	disolacis and pre-modulastic
				Malm, Methods in Enzymol	conditions, such as, for example,
				216:362-368 (1992); Henthorn	hyperplasia, metaplasia, and/or
			•	et al., Proc Natl Acad Sci USA	dysplasia. Preferred indications
				85:6342-6346 (1988); Flavell et	include anemia, pancytopenia,
				al., Cold Spring Harb Symp	leukopenia, thrombocytopenia,
				Quant Biol 64:563-571 (1999);	leukemias, Hodgkin's disease,
				Rodriguez-Palmero et al., Eur J	acute lymphocytic anemia
				Immunol 29(12):3914-3924	(ALL), plasmacytomas, multiple
				(1999); Zheng and Flavell, Cell	myeloma, Burkitt's lymphoma,
				89(4):587-596 (1997); and	arthritis, AIDS, granulomatous
				Henderson et al., Mol Cell Biol	disease, inflammatory bowel
				14(6):4286-4294 (1994), the	disease, sepsis, neutropenia,
				contents of each of which are	neutrophilia, psoriasis,
				herein incorporated by reference	suppression of immune
				in its entirety. Mast cells that	reactions to transplanted organs
				may be used according to these	and tissues, hemophilia,
				assays are publicly available	hypercoagulation, diabetes
				(e.g., through the ATCC).	mellitus, endocarditis,
				Exemplary human mast cells	meningitis, and Lyme Disease.
				that may be used according to	
				these assays include the HMC-1	
				cell line, which is an immature	
				human mast cell line established	
				from the peripheral blood of a	
				patient with mast cell leukemia,	
				and exhibits many	
				characteristics of immature mast	
				cells.	
	НЕВDQ91	522		This reporter assay measures	Highly preferred indications
108			transcription through	activation of the NFAT	include allergy, asthma, and

rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under	"Infectious Disease"), and inflammation and inflammatory	disorders. Preferred indications also include blood disorders	(e.g., as described below under "Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and immunodeficiencies	(e.g., as described below).		neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary tract cancers	and/or as described below under	"Hyperproliferative Disorders").	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or
signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to eytokine and	chemokine production. Assays for the activation of	transcription through the Nuclear Factor of Activated T	cells (NFAT) response element are well-known in the art and	may be used or routinely	modified to assess the ability of	polypeptides of the invention (including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in immunomodulatory	functions. Exemplary assays for	transcription through the NFAT	response element that may be	used or routinely modified to	test NFAT-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA
NFAT response element in immune cells (such as mast	cells).				•										•										
																			_		_				

dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include inflammation (acute and chronic), restnosis, athma and allergy. Highly preferred indications include inflammation and inflammatory
85:6342-6346 (1988); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
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transcription through	transcription through the CD28	embodiment of the invention
CD28 response	response element are well-	includes a method for
element in immune	known in the art and may be	stimulating T cell proliferation.
cells (such as T-	used or routinely modified to	An alternative highly preferred
cells).	assess the ability of	embodiment of the invention
	polypeptides of the invention	includes a method for inhibiting
	(including antibodies and	T cell proliferation. A highly
	agonists or antagonists of the	preferred embodiment of the
	invention) to stimulate IL-2	invention includes a method for
	expression in T cells.	activating T cells. An alternative
	Exemplary assays for	highly preferred embodiment of
	transcription through the CD28	the invention includes a method
	response element that may be	for inhibiting the activation of
	used or routinely modified to	and/or inactivating T cells.
	test CD28-response element	A highly preferred embodiment
	activity of polypeptides of the	of the invention includes a
	invention (including antibodies	method for stimulating (e.g.,
	and agonists or antagonists of	increasing) IL-2 production. An
	the invention) include assays	alternative highly preferred
	disclosed in Berger et al., Gene	embodiment of the invention
	66:1-10 (1998); Cullen and	includes a method for inhibiting
	Malm, Methods in Enzymol	(e.g., reducing) IL-2 production.
	216:362-368 (1992); Henthorn	Additional highly preferred
	et al., Proc Natl Acad Sci USA	indications include
	85:6342-6346 (1988); McGuire	inflammation and inflammatory
	and Iacobelli, J Immunol	disorders. Highly preferred
	159(3):1319-1327 (1997); Parra	indications include autoimmune
	et al., J Immunol 166(4):2437-	diseases (e.g., rheumatoid
	2443 (2001); and Butscher et al.,	arthritis, systemic lupus
	J Biol Chem 3(1):552-560	erythematosis, multiple sclerosis
	(1998), the contents of each of	and/or as described below),
	which are herein incorporated	immunodeficiencies (e.g., as
	by reference in its entirety. T	described below), boosting a T

cell-mediated immune response, and suppressing a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma,	leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g.,	metastatic renal cell carcinoma), leukemia, lymphoma (e.g. T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection	(e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly
cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the	SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.			

					preferred indication is AIDS.
					Additional highly preferred
					indications include suppression
	-		-		of immune reactions to
			-		transplanted organs and/or
			, ,		tissues, uveitis, psoriasis, and
		,,,			tropical spastic paraparesis.
					Preferred indications include
		,,,			blood disorders (e.g., as
					described below under "Immune
				,	Activity", "Blood-Related
			•		Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications also
					include anemia, pancytopenia,
			•		leukopenia, thrombocytopenia,
			-		Hodgkin's disease, acute
		-			lymphocytic anemia (ALL),
					plasmacytomas, multiple
	-				myeloma, Burkitt's lymphoma,
					arthritis, granulomatous disease,
	-				inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
_					meningitis, Lyme Disease,
					asthma and allergy.
	HFBFR46	523	Activation of	Assays for the activation of	A highly preferred indication is
109			transcription through	transcription through the cAMP	obesity and/or complications
		•	cAMP response	response element are well-	associated with obesity.
			element (ČRE) in	known in the art and may be	Additional highly preferred

	2011	nead or routinely modified to	indications include weight loss
	pre-aupocytes.	assess the ability of	or alternatively, weight gain.
		polypeptides of the invention	An additional highly preferred
		(including antibodies and	indication is diabetes mellitus.
		agonists or antagonists of the	An additional highly preferred
		invention) to increase cAMP,	indication is a complication
		regulate CREB transcription	associated with diabetes (e.g.,
		factors, and modulate	diabetic retinopathy, diabetic
		expression of genes involved in	nephropathy, kidney disease
		a wide variety of cell functions.	(e.g., renal failure, nephropathy
-		For example, a 3T3-L1/CRE	and/or other diseases and
		reporter assay may be used to	disorders as described in the
		identify factors that activate the	"Renal Disorders" section
		cAMP signaling pathway.	below), diabetic neuropathy,
		CREB plays a major role in	nerve disease and nerve damage
		adipogenesis, and is involved in	(e.g., due to diabetic
		differentiation into adipocytes.	neuropathy), blood vessel
		CRE contains the binding	blockage, heart disease, stroke,
		sequence for the transcription	impotence (e.g., due to diabetic
		factor CREB (CRE binding	neuropathy or blood vessel
		protein). Exemplary assays for	blockage), seizures, mental
		transcription through the cAMP	confusion, drowsiness,
		response element that may be	nonketotic hyperglycemic-
		used or routinely modified to	hyperosmolar coma,
	_	test cAMP-response element	cardiovascular disease (e.g.,
		activity of polypeptides of the	heart disease, atherosclerosis,
		invention (including antibodies	microvascular disease,
		and agonists or antagonists of	hypertension, stroke, and other
		the invention) include assays	diseases and disorders as
		disclosed in Berger et al., Gene	described in the "Cardiovascular
		66:1-10 (1998); Cullen and	Disorders" section below),
		Malm, Methods in Enzymol	dyslipidemia, endocrine
		216:362-368 (1992); Henthorn	disorders (as described in the

-	et	al., Mol Cell Biol 20(3):1008- impairment (e.g., diabetic	 J Biol Chem 273:917-923 ulcers and impaired wound	oh of	 by reference in its entirety. Pre- as described in the "Infectious	 according to these assays are especially of the urinary tract	lgh	 contracture). Additional highly contracture). Additional highly	 be used according to these complications associated with	assays include 3T3-L1 cells. insulin resistance.	3T3-L1 is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	523 Activation of	transcription through activation of the GATA-3		e human mast cell line. Activation		been linked to cytokine and	•
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inflammation and inflammatory disorders. Preferred indications	(e.g., as described below under	"Immune Activity", "Blood-	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described			Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary tract cancers	and/or as described below under	"Hyperproliferative Disorders").	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia
for the activation of transcription through the	GATA3 response element are well-known in the art and may	be used or routinely modified to	assess the ability of	(including antibodies and	agonists or antagonists of the	invention) to regulate GATA3	transcription factors and	modulate expression of mast	cell genes important for immune	response development.	Exemplary assays for	transcription through the	GATA3 response element that	may be used or routinely	modified to test GATA3-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell et	al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur J
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(ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section
Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies.
	Stimulation of insulin secretion from pancreatic beta cells.
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include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers,	such as, leukemia, lymphoma, prostate, breast, lung, colon, nancreatic, esophageal, stomach,		include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example,				disease, acute lymphocytic	anemia (ALL), piasmacytolitas, multiple myeloma, Burkitt's	lymphoma, granulomatous disease, inflammatory bowel	disease, sepsis,	psoriasis, suppression of immune	and tissues, endocarditis,	meningitis, and Lyme Disease.
66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Froc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem	272(49):30806-30811 (1997); Chang et al., Mol Cell Biol	Fraser et al., Eur J Immunol 29(3):838-844 (1999), the	herein incorporated by reference in its entirety. Human T cells	that may be used according to these assays are publicly	available (e.g., through the	cells that may be used according	to these assays include the SUPT cell line, which is an IL-2	and IL-4 responsive suspension-							
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A highly preferred embodiment of the invention	includes a method for	stimulating T cell proliferation.	An alternative highly preferred	embodiment of the invention	includes a method for inhibiting	T cell proliferation. A highly	preferred embodiment of the	invention includes a method for	activating T cells. An alternative	highly preferred embodiment of	the invention includes a method	for inhibiting the activation of	and/or inactivating T cells.	A highly preferred embodiment	of the invention includes a	method for stimulating (e.g.,	increasing) IL-2 production. An	alternative highly preferred	embodiment of the invention	includes a method for inhibiting	(e.g., reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and inflammatory	disorders. Highly preferred	indications include autoimmune	diseases (e.g., rheumatoid			and/or as described below),	immunodeficiencies (e.g., as
Assays for the activation of transcription through the CD28	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate IL-2	expression in T cells.	Exemplary assays for	transcription through the CD28	response element that may be	used or routinely modified to	test CD28-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); McGuire	and Jacobelli, J Immunol	159(3):1319-1327 (1997); Parra	et al., J Immunol 166(4):2437-	2443 (2001); and Butscher et al.,	J Biol Chem 3(1):552-560	(1998), the contents of each of	which are herein incorporated
Activation of	CD28 response	element in immune	cells (such as T-	cells).	.(2																										
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described below), boosting a T cell-mediated immune response,	and suppressing a T cell-	mediated immune response.	Highly preferred indications	include neoplastic diseases (e.g.,	melanoma, renal cell carcinoma,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Highly preferred indications	include neoplasms and cancers,	such as, for example, melanoma	(e.g., metastatic melanoma),	renal cell carcinoma (e.g.,	metastatic renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. A highly preferred	indication includes infection	(e.g., AIDS, tuberculosis,	infections associated with	granulomatous disease, and	osteoporosis, and/or as	described below under
by reference in its entirety. T	to these assays are publicly	available (e.g., through the	ATCC). Exemplary human T	cells that may be used according	to these assays include the	SUPT cell line, which is a	suspension culture of IL-2 and	II4 responsive T cells.																							
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"Infections Disease"). A highly	preferred indication is AIDS.	Additional highly preferred	indications include suppression	of immune reactions to	transplanted organs and/or	tissues, uveitis, psoriasis, and	tropical spastic paraparesis.	Preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma and allergy.	Highly preferred indications	include blood disorders (e.g., as	described below under "Immune
																													Assays for the activation of	transcription through the	Nuclear Factor of Activated T
			-																										A crimation of	transcription through	NFAT response
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Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").	Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, multiple sclerosis and/or as described below),	immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response,	and suppressing a T cell- mediated immune response.	Additional highly preferred indications include	inflammation and inflammatory	disorders. An additional inging preferred indication is infection	(e.g., an infectious disease as	described below under "Infectious Disease").	Preferred indications include	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").		for example, leukemia,	lymphoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,
cells (NFAT) response element are well-known in the art and may be used or routinely	modified to assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to regulate NFAT transcription factors and	modulate expression of genes involved in immunomodulatory functions. Exemplary assays for	transcription through the NFAT response element that may be	used or routinely modified to	activity of polypeptides of the	invention (including antibodies and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer et al Int I Riochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem
element in immune cells (such as T-cells).																	,	
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live pref pref pref pref pref pref pref pre	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related
268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Activation of transcription through NFKB response element in immune cells (such as Tells).
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Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An additional	highly preferred indication is	infection (e.g., AIDS, and/or an	infectious disease as described	below under "Infectious	Disease"). Highly preferred	indications include neoplastic	diseases (e.g., melanoma,	leukemia, lymphoma, and/or as	described below under	""Hyperproliferative Disorders").	Highly preferred indications	include neoplasms and cancers,	such as, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or
Gincluding antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the NFKB	response element that may be	used or rountinely modified to	test NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by reference	in its entirety. T cells that may	he used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell
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dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	A highly preferred indication is allergy. highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include
line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary
	Activation of transcription through STAT6 response element in immune cells (such as Tcells).
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autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and immunodeficiencies	(e.g., as described below).	Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Other preferred indications	include benign dysproliferative			hyperplasia, metaplasia, and/or	dysplasia.	Preferred indications include			Hodgkin's disease, acute			myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel
assays for transcription through	that may be used or routinely	modified to test STAT6	response element activity of the	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Georas et	al Blood 92(12):4529-4538	(1998); Moffatt et al.,	Transplantation 69(7):1521-	1523 (2000); Curiel et al., Eur J	[mmunol 27(8):1982-1987	(1997); and Masuda et al., J Biol	Chem 275(38):29331-29337	(2000), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4
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disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious	-	nignly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, todow, parcreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include
responsive T cells.		Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that
	SEAP in ATP-3T3- L1	Activation of transcription through GAS response element in immune cells (such as Teells).
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idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders").
	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
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Preferred indications include autoimmune diseases (e.g.,	rheumatoid artinrius, systemile lupus erythematosis, multiple	sclerosis and/or as described	below) and immunodeficiencies	(e.g., as described below). Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary tract cancers	and/or as described below under	"Hyperproliferative Disorders").	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred indications	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune
(including antibodies and agonists or antagonists of the	invention) to regulate GATA3 transcription factors and	modulate expression of mast	cell genes important for immune	response development.	transcription through the	GATA3 response element that	may be used or routinely	modified to test GATA3-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell et	al Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur J	Immunol 29(12):3914-3924	(1999); Zheng and Flavell, Cell	89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by reference
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reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.		-	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic
in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.			Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also
	IgG in Human B	IgG in Human B cells SAC	Stimulation of insulin secretion from pancreatic beta cells.
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by certain proteins/peptides, and blockage, heart disease, stocke, component in diabetes. Exemplary assays that may be restricted; Exemplary assays that may be be polypeptides of the invention of insulin socretion (from panceatic cells, adminstored in hyperosmoliar coma, agoints or antagonists of the invention) include assays disclosed in: Ahren, B., et al., hyperosmoliar coma, al., Endocrinology, 11, M., et al., FEBS, Lett., at al., FEBS, Lett., at al., FEBS, Lett., at al., FEBS, Lett., at al., Endocrinology, 13, m., et al., physiol., 237-9 (1997); Kim, glassies and disorders as and eigenders of white plates and concludent according to these says are publicly available (e.g., diabetic supplicity available (e.g., et align); perceivation insentiered. Banchetel and the art disease, altheroscierosis, invention) include assays and signorders as and signorders as and eigenders and effective and physiol., 237-9 (1997); Kim, glassies and disorders as a described in the "Cardiovascular Bonorderular Socreening, 4:193-194. Banchetel and the art of
by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antigaonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., ER95-66 (1999); Li, M., et al., ER95-66 (1999); Li, M., et al., ER8 Lett, 377(2):237-9 (1997); Kim, K.H., et al., EBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) andor may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. Ansays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells.

				isolated from an X-ray induced rat transplantable insulinoma.	Additional highly preferred indications include weight loss
				These cells retain characteristics	or alternatively, weight gain.
				typical of native pancreatic beta	Aditional highly preferred
				cells including glucose inducible	indications are complications
				insulin secretion. References:	associated with insulin
				Asfari et al. Endocrinology	resistance.
				1992 130:167.	
	HEI AT35	575	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred embodiment
	CHUTTI			by T cells and has strong effects	of the invention includes a
111				on B cells. IL-6 participates in	method for stimulating (e.g.,
				IL-4 induced IgE production	increasing) IL-6 production. An
				and increases IgA production	alternative highly preferred
				(IgA plays a role in mucosal	embodiment of the invention
				immunity). IL-6 induces	includes a method for inhibiting
				cytotoxic T cells. Deregulated	(e.g., reducing) IL-6 production.
				expression of IL-6 has been	A highly preferrred indication is
				linked to autoimmune disease,	the stimulation or enhancement
				plasmacytomas, myelomas, and	of mucosal immunity. Highly
				chronic hyperproliferative	preferred indications include
				diseases. Assays for	blood disorders (e.g., as
_				immunomodulatory and	described below under "Immune
				differentiation factor proteins	Activity", "Blood-Related
				produced by a large variety of	Disorders", and/or
				cells where the expression level	"Cardiovascular Disorders"),
				is strongly regulated by	and infection (e.g., as described
				cytokines, growth factors, and	below under "Infectious
				hormones are well known in the	Disease"). Highly preferred
				art and may be used or routinely	indications include autoimmune
				modified to assess the ability of	diseases (e.g., rheumatoid
		_		polypeptides of the invention	arthritis, systemic lupus
			_	(including antibodies and	erythematosis, multiple sclerosis

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and/or as described below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response and	alternatively suppressing a B	cell-mediated immune response.	Highly preferred indications	include inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	Iymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal, stomach,	brain, liver and urinary cancer.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or
agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and the	stimulation and upregulation of	T cell proliferation and	functional activities. Such	assays that may be used or	routinely modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using
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dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infectious disease as described below under "Infectious Disease").		Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-
techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.		Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of
	SEAP in SW480	Activation of transcription through AP1 response element in immune cells (such as T-cells).
	525	526
	HELAT35	HELBU54
	=	112

Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications	include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers,	<u> </u>	include benign dysproliterative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis,
the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element	activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66.1-10 (1988). Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:4342-6346 (1988); Rellahan	et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol	29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these	assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent

asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A nignly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious
suspension-culture cell line with cytotoxic activity.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and
	Production of IL-6
	527
	HEMEY47
	113

Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid	arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Highly preferred indications also	include boosting a B cell- mediated immune response and alternatively suppressing a B	cell-mediated immune response. Highly preferred indications include inflammation and	inflammatory disorders.Additional highly	preferred indications include asthma and allergy. Highly preferred indications include	neoplastic diseases (e.g., myeloma, plasmacytoma,	leukemia, lymphoma, melanoma, and/or as described	Disorders"). Highly preferred indications include neoplasms	and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer.
hormones are well known in the art and may be used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) to mediate immunomodulation and differentiation and modulate T	cell proliferation and function. Exemplary assays that test for immunomodulatory proteins	evaluate the production of cytokines, such as IL-6, and the stimulation and unregulation of	T cell proliferation and functional activities. Such	assays that may be used or routinely modified to test	differentiation activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the	disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	(2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of

				which are herein incorporated	Other preferred indications
				by reference in its entirety.	include benign dysproliferative
-				Human dendritic cells that may	disorders and pre-neoplastic
			,	be used according to these	conditions, such as, for example,
				assays may be isolated using	hyperplasia, metaplasia, and/or
				techniques disclosed herein or	dysplasia. Preferred indications
				otherwise known in the art.	include anemia, pancytopenia,
				Human dendritic cells are	leukopenia, thrombocytopenia,
				antigen presenting cells in	Hodgkin's disease, acute
				suspension culture, which, when	lymphocytic anemia (ALL),
				activated by antigen and/or	multiple myeloma, Burkitt's
				cytokines, initiate and	lymphoma, arthritis, AIDS,
				upregulate T cell proliferation	granulomatous disease,
				and functional activities.	inflammatory bowel disease,
				1	sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted organs
					and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
-					infectious disease as described
					below under "Infectious
					Disease").
	HEMEY47	527	MCP-1 in HUVEC		
113			111/7 1 1		
114	HEOMC46	528	SEAP in Jurkat/IL4 promoter		
	HEOMC46	528	SEAP in Jurkat/IL4		
	200000				

HEPBA14 529	NK16/STAT6 Activation of transcription through		
529	Activation of transcription through		
·		Assays for the activation of transcription through the AP1	Preferred indications include neoplastic diseases (e.g., as
· · ·	API response	response element are known in	described below under
<u> </u>	element in immune	the art and may be used or	"Hyperproliferative Disorders"),
·	cells (such as T-	routinely modified to assess the	blood disorders (e.g., as
·	cells).	ability of polypeptides of the	described below under "Immune
	`	invention (including antibodies	Activity", "Cardiovascular
<u> </u>		and agonists or antagonists of	Disorders", and/or "Blood-
<u>.</u>		the invention) to modulate	Related Disorders"), and
·		growth and other cell functions.	infection (e.g., an infectious
_		Exemplary assays for	disease as described below
		transcription through the AP1	under "Infectious Disease").
		response element that may be	Highly preferred indications
-		used or routinely modified to	include autoimmune diseases
		test AP1-response element	(e.g., rheumatoid arthritis,
		activity of polypeptides of the	systemic lupus erythematosis,
_		invention (including antibodies	multiple sclerosis and/or as
	•	and agonists or antagonists of	described below) and
		the invention) include assays	immunodeficiencies (e.g., as
	•	disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
-		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988); Rellahan	also include neoplastic diseases
		et al., J Biol Chem	(e.g., leukemia, lymphoma,
		272(49):30806-30811 (1997);	and/or as described below under
		Chang et al., Mol Cell Biol	"Hyperproliferative Disorders").

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				Fraser et al., Eur J Immunol	include neoplasms and cancers,
				29(3):838-844 (1999), the	such as, leukemia, lymphoma,
_	_			contents of each of which are	prostate, breast, lung, colon,
				herein incorporated by reference	pancreatic, esophageal, stomach,
		-		in its entirety. T cells that may	brain, liver, and urinary cancer.
				be used according to these	Other preferred indications
				assays are publicly available	include benign dysproliferative
_				(e.g., through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for example,
		1		may be used according to these	hyperplasia, metaplasia, and/or
			-	assays include the CTLL cell	dysplasia. Preferred
				line, which is an IL-2 dependent	indications include arthritis,
				suspension-culture cell line with	asthma, AIDS, allergy, anemia,
-				cytotoxic activity.	pancytopenia, leukopenia,
				•	thrombocytopenia, Hodgkin's
					disease, acute lymphocytic
					anemia (ALL), plasmacytomas,
					multiple myeloma, Burkitt's
					lymphoma, granulomatous
					disease, inflammatory bowel
_		,			disease, sepsis, psoriasis,
					suppression of immune
					reactions to transplanted organs
					and tissues, endocarditis,
					meningitis, and Lyme Disease.
	HEOAH80	530	Activation of	Kinase assay. Kinase assays,	A highly preferred
16))	Natural Killer Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
	.,,		Pathway.	transduction that regulate cell	stimulating natural killer cell
			•	proliferation or differentiation	proliferation. An alternative
	•			are well known in the art and	highly preferred embodiment of

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the invention includes a method for inhibiting natural killer cell	proliferation. A highly	preferred embodiment of the	invention includes a method for	stimulating natural killer cell	differentiation. An alternative	highly preferred embodiment of	the invention includes a method	for inhibiting natural killer cell	differentiation. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	w. "Hyperproliferative Disorders"),	blood disorders (e.g., as	described below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity") and infections (e.g.,	as described below under	"Infectious Disease").	Preferred indications include	blood disorders (e.g., as	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	Include autoimmine diseases
may be used or routinely	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to promote or inhibit	cell proliferation, activation, and	differentiation. Exemplary	assays for ERK kinase activity	that may be used or routinely	modified to test ERK kinase-	induced activity of polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention)	include the assays disclosed in	Forrer et al., Biol Chem 379(8-	9):1101-1110 (1998); Kyriakis	JM, Biochem Soc Symp 64:29-	48 (1999); Chang and Karin,	Nature 410(6824):37-40 (2001);	and Cobb MH, Prog Biophys	Mol Biol 71(3-4):479-500	(1999); the contents of each of	which are herein incorporated	by reference in its entirety.	Natural killer cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC). Exemplary	natural killer cells that may be	used according to these assays	List the birmon notine billor
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(e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional highly preferred indications	include inflammation and inflammatory disorders. Highly preferred indications	also include cancers such as, kidney, melanoma, prostate, breast lung colon, pancreatic,	esophageal, stomach, brain, liver, urinary cancer, lymphoma	and leukemias. Other preferred indications include benign	dysproliferative disorders and	as, for example, hyperplasia,	metaplasia, and/or dysplasia. Other highly preferred	indications include,	leukemias, Hodgkin's disease,	acute lymphocytic anemia (ALL), arthritis, asthma, AIDS,	granulomatous disease,	sepsis, psoriasis, immune	reactions to transplanted organs	and tissues, endocarditis,	meningitis, Lyme Disease, and
cell lines (for example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells.																
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					allergies.
	HETDW58	531	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred embodiment
117				by T cells and has strong effects	of the invention includes a
<u> </u>				on B cells. IL-6 participates in	method for stimulating (e.g.,
				IL-4 induced IgE production	increasing) IL-6 production. An
				and increases IgA production	alternative highly preferred
				(IgA plays a role in mucosal	embodiment of the invention
				immunity). IL-6 induces	includes a method for inhibiting
				cytotoxic T cells. Deregulated	(e.g., reducing) IL-6 production.
				expression of IL-6 has been	A highly preferrred indication is
		_		linked to autoimmune disease,	the stimulation or enhancement
				plasmacytomas, myelomas, and	of mucosal immunity. Highly
				chronic hyperproliferative	preferred indications include
				diseases. Assays for	blood disorders (e.g., as
				immunomodulatory and	described below under "Immune
			***	differentiation factor proteins	Activity", "Blood-Related
				produced by a large variety of	Disorders", and/or
				cells where the expression level	"Cardiovascular Disorders"),
	·-			is strongly regulated by	and infection (e.g., as described
				cytokines, growth factors, and	below under "Infectious
				hormones are well known in the	Disease"). Highly preferred
				art and may be used or routinely	indications include autoimmune
				modified to assess the ability of	diseases (e.g., rheumatoid
	-			polypeptides of the invention	arthritis, systemic lupus
				(including antibodies and	erythematosis, multiple sclerosis
				agonists or antagonists of the	and/or as described below) and
				invention) to mediate	immunodeficiencies (e.g., as
				immunomodulation and	described below). Highly
				differentiation and modulate T	preferred indications also
				cell proliferation and function.	include boosting a B cell-
_	_			Exemplary assays that test for	mediated immune response and
				immunomodulatory proteins	alternatively suppressing a B

granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammatory
upregulate T cell proliferation and functional activities.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for
	Production of MCP-1
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	HETDW58
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disorders. Preferred indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Kelated	Disorders', and/or	Tr. 11 General Disolucis J.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs	and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis (bacterial and viral),	Lyme Disease, asthma, and
immunomodulatory proteins evaluate the production of cell	surface markers, such as	monocyte chemoattractant	protein (MCP), and the	activation of monocytes and I	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and Eremin,	J R Coll Surg Ednb 45(1):9-19	(2001); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in
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allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related
suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins
	Production of 1L-6
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	HETEY67
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			for vigitation of the variety of	Disorders" and/or
		-	produced by a range variety of	"Cardiovascular Disorders").
			is strongly regulated by	and infection (e.g., as described
	-		cytokines, growth factors, and	below under "Infectious
			hormones are well known in the	Disease"). Highly preferred
			art and may be used or routinely	indications include autoimmune
			modified to assess the ability of	diseases (e.g., rheumatoid
			polypeptides of the invention	arthritis, systemic lupus
			(including antibodies and	erythematosis, multiple sclerosis
<u> </u>			agonists or antagonists of the	and/or as described below) and
			invention) to mediate	immunodeficiencies (e.g., as
			immunomodulation and	described below). Highly
_			differentiation and modulate T	preferred indications also
			cell proliferation and function.	include boosting a B cell-
			Exemplary assays that test for	mediated immune response and
		_	immunomodulatory proteins	alternatively suppressing a B
			evaluate the production of	cell-mediated immune response.
_			eytokines, such as IL-6, and the	Highly preferred indications
			stimulation and upregulation of	include inflammation and
			T cell proliferation and	inflammatory
			functional activities. Such	disorders.Additional highly
	-		assays that may be used or	preferred indications include
			routinely modified to test	asthma and allergy. Highly
	-		immunomodulatory and	preferred indications include
			diffferentiation activity of	neoplastic diseases (e.g.,
-	-		polypeptides of the invention	myeloma, plasmacytoma,
			(including antibodies and	leukemia, lymphoma,
	_		agonists or antagonists of the	melanoma, and/or as described
			invention) include assays	below under "Hyperproliferative
			disclosed in Miraglia et al., J	Disorders"). Highly preferred
	_		Biomolecular Screening 4:193-	indications include neoplasms
	-		204(1999); Rowland et al.,	and cancers, such as, myeloma,
			"Lymphocytes: a practical	plasmacytoma, leukemia,

nma, and ng, colon, geal, stomach, nary cancer. lications proliferative eoplastic d indications ncytopenia, acute ia (ALL), Burkitt's s, AIDS, sase, el disease, el disease, nune anted organs ohilia, diabetes titis, me Disease. rred ion (e.g., an as described tions	opinjon; onc;
lymphoma, melanoma, and prostate, breast, lung, colon, bancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious	Disease").
approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	A 6
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blood disorders (e.g., as described below under "Immune Activity", "Blood-Related	Disorders", and/or "Cardiovascular Disorders"),	and infection (e.g., an infectious disease as described below	under "Infectious Disease"). Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), illilliallouellelelles	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and inflammatory	disorders. Highly preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma (e.g., T cell	lymphoma, Burkitt's	lymphoma, non-Hodgkins	lymphoma, Hodgkin"s disease),
transcription through transcription through the cAMP cAMP response response element in immune known in the art and may be	used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to increase cAMP	bind to CREB transcription	factor, and modulate expression	of genes involved in a wide	variety of cell functions.	Exemplary assays for	response element that may be	used or routinely modified to	test cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated
transcription through cAMP response element in immune	cells (such as T-cells).																			, an						
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melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes melitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as
by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to
	Activation of transcription through NFKB response element in immune cells (such as T-
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	HFCDW95
	119

described below under "Immune	vention Activity", "Blood-Related	and Disorders", and/or				of (e.g., rheumatoid arthritis,	les.	multiple sclerosis and/or as		may be immunodeficiencies (e.g., as	diffed to described below). An additional	<u></u>	es of the infection (e.g., AIDS, and/or an	S	onists of below under "Infectious		al., Gene indications include neoplastic	in and diseases (e.g., melanoma,					105-117 include neoplasms and cancers,), the renal cell carcinoma, leukemia,			plary esophageal, stomach, brain,		-		o through disorders and pre-neoplastic
cells). assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the NFKB	response element that may be	used or rountinely modified to	test NFKB-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by reference	in its entirety. Exemplary	human T cells, such as the	MOLT4, that may be used	according to these assays are	hrough a place in through
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conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic	anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,	neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include
the ATCC).		·	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative
			Production of IL-6
			534
			HFCFD04
			120

dispuse Assessing for Hood disorders (e.g. 88	-	immunomodulatory and described below under "Immune	differentiation factor proteins Activity", "Blood-Related	produced by a large variety of Disorders", and/or	 is strongly regulated by and infection (e.g., as described	rs, and	hormones are well known in the Disease"). Highly preferred	art and may be used or routinely indications include autoimmune	modified to assess the ability of diseases (e.g., rheumatoid	(including antibodies and erythematosis, multiple sclerosis	the	invention) to mediate immunodeficiencies (e.g., as	pu	differentiation and modulate T preferred indications also	Exemplary assays that test for mediated immune response and	immunomodulatory proteins alternatively suppressing a B	evaluate the production of cell-mediated immune response.	cytokines, such as IL-6, and the Highly preferred indications	stimulation and upregulation of include inflammation and	T cell proliferation and inflammatory	functional activities. Such disorders. Additional highly	assays that may be used or preferred indications include	routinely modified to test asthma and allergy. Highly	immunomodulatory and preferred indications include	diffferentiation activity of neoplastic diseases (e.g.,	polypeptides of the invention myeloma, plasmacytoma,	 the	
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indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and	prostate, oreast, rung, coron, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia.	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune	reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below, under "Infectious"
Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	(2000); and Verhasself et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art	Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or	cytokines, initiate and upregulate T cell proliferation and functional activities.	

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HFCFD04	534	SEAP in HIB/CRE		
HFEAY59	535	Apoptosis Apoptosis		A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating method for stimulating
	HFEAY59		535	535 Endothelial Cell Apoptosis

highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a	method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under	"Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and	atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular,
of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available	(e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that	include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	

disorders that affect vessels such	as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or	lymphatics). Highly preferred are indications that stimulate angiogenesis and/or	cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	Highly preferred indications include antiangiogenic activity	to treat solid tumors, leukemias,	retinal disorders. Highly preferred indications include	neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma	(capillary and cavernous), glomus tumors, telangiectasia,	bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma,	lymphangioma, lymphangiosarcoma. Highly	preferred indications also include cancers such as, prostate, breast, lung, colon,
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	pancreatic, esophageal, stomach,	brain, liver, and urinary cancer.	Preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Highly preferred	indications also include arterial	disease, such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud''s disease	and Reynaud"s phenomenom,	aneurysms, restenosis; venous	and lymphatic disorders such as	thrombophlebitis, lymphangitis,	and lymphedema; and other	vascular disorders such as	peripheral vascular disease, and	cancer. Highly preferred	indications also include trauma	such as wounds, burns, and	injured tissue (e.g., vascular	injury such as, injury resulting	from balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	1
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					diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
	HFEAY59	535	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
121			IFINGAMMA USING A	system and is considered to be a	includes a method for
				proinflammatory cytokine.	stimulating the production of
				IFNg promotes TH1 and	IFNg. An alternative highly
				inhibits TH2 differentiation;	preferred embodiment of the
				promotes IgG2a and inhibits IgE	invention includes a method for
				secretion; induces macrophage	inhibiting the production of
				activation; and increases MHC	IFNg. Highly preferred
				expression. Assays for	indications include blood
				immunomodulatory proteins	disorders (e.g., as described
				produced by T cells and NK	below under "Immune
				cells that regulate a variety of	Activity", "Blood-Related
				inflammatory activities and	Disorders", and/or
				inhibit TH2 helper cell functions	"Cardiovascular Disorders"),
				are well known in the art and	and infection (e.g., viral
				may be used or routinely	infections, tuberculosis,
				modified to assess the ability of	infections associated with
				polypeptides of the invention	chronic granulomatosus disease
				(including antibodies and	and malignant osteoporosis,
				agonists or antagonists of the	and/or as described below under
				invention) to mediate	"Infectious Disease"). Highly
				immunomodulation, regulate	preferred indications include
				inflammatory activities,	autoimmune disease (e.g.,
-				modulate TH2 helper cell	rheumatoid arthritis, systemic
				function, and/or mediate	lupus erythematosis, multiple
				humoral or cell-mediated	sclerosis and/or as described
				immunity. Exemplary assays	below), immunodeficiency (e.g.,
				that test for immunomodulatory	as described below), boosting a

		motoing avaluate the production	T cell-mediated immune
		of cytokines such as Interferon	response, and suppressing a T
	-	gamma (IFNg), and the	cell-mediated immune response.
		activation of T cells. Such	Additional highly preferred
		assays that may be used or	indications include
		routinely modified to test	inflammation and inflammatory
		immunomodulatory activity of	disorders. Additional preferred
		polypeptides of the invention	
		(including antibodies and	pulmonary fibrosis. Highly
		agonists or antagonists of the	preferred indications include
		invention) include the assays	neoplastic diseases (e.g.,
		disclosed in Miraglia et al., J	leukemia, lymphoma,
		Biomolecular Screening 4:193-	melanoma, and/or as described
		204 (1999); Rowland et al.,	below under "Hyperproliferative
		"Lymphocytes: a practical	Disorders"). Highly preferred
		approach" Chapter 6:138-160	indications include neoplasms
		(2000); Gonzalez et al., J Clin	and cancers, such as, for
		Lab Anal 8(5):225-233 (1995);	example, leukemia, lymphoma,
		Billiau et al., Ann NY Acad Sci	melanoma, and prostate, breast,
		856:22-32 (1998); Boehm et al.,	lung, colon, pancreatic,
		Annu Rev Immunol 15:749-795	esophageal, stomach, brain,
		(1997), and Rheumatology	liver and urinary cancer. Other
		(Oxford) 38(3):214-20 (1999),	preferred indications include
		the contents of each of which	benign dysproliferative
		are herein incorporated by	disorders and pre-neoplastic
		reference in its entirety. Human	conditions, such as, for example,
		T cells that may be used	hyperplasia, metaplasia, and/or
		according to these assays may	dysplasia. Preferred
		be isolated using techniques	indications include anemia,
		disclosed herein or otherwise	pancytopenia, leukopenia,
		known in the art. Human T	thrombocytopenia, Hodgkin's
		cells are primary human	disease, acute lymphocytic
		lymphocytes that mature in the	anemia (ALL), plasmacytomas,

multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by
• .	Production of ICAM-1
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	HFEAY59
	121

-	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting or inhibiting immune cell proliferation. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as
reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
	536
	HFEBO17
	122

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described below under "Hyperproliferative Disorders"). Highly preferred indications include boosting an eosinophil-	mediated immune response, and suppressing an eosinophil-	mediated immune response.														-									-		
Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang	and Narini, Ivature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in the	late stage of allergic reactions;	they are recruited to tissues and	mediate the inflammatory	response of late stage allergic	reaction. Moreover, exemplary	assays that may be used or	routinely modified to assess the	ability of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils include	assays disclosed and/or cited in:	Zhang JP, et al., "Role of	caspases in dexamethasone-	induced apoptosis and activation	of c-Jun NH2-terminal kinase
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	Highly preferred indications include eosinophilia, asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related
and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate
	Regulation of viability or proliferation of immune cells (such as human eosinophil EOL-1 cells).
	537
	HFGAJ16
	123

				viability and proliferation of	Disorders"), autoimmune
				eosinophil cells and cell lines.	diseases (e.g., rheumatoid
				For example, the CellTiter-Gloô	arthritis, systemic lupus
				Luminescent Cell Viability	erythematosis, Crohn's disease,
				Assay (Promega Corp.,	multiple sclerosis and/or as
				Madison, WI, USA) can be	described below),
				used to measure the number of	immunodeficiencies (e.g., as
				viable cells in culture based on	described below). Highly
				quantitation of the ATP present	preferred indications also
				which signals the presence of	include boosting or inhibiting
				metabolically active cells.	immune cell proliferation.
				Eosinophils are a type of	Preferred indications include
	-			immune cell important in	neoplastic diseases (e.g.,
				allergic responses; they are	leukemia, lymphoma, and/or as
				recruited to tissues and mediate	described below under
				the inflammtory response of late	"Hyperproliferative Disorders").
				stage allergic reaction.	Highly preferred indications
				Eosinophil cell lines that may be	include boosting an eosinophil-
				used according to these assays	mediated immune response, and
				are publicly available and/or	suppressing an eosinophil-
				may be routinely generated.	mediated immune response.
				Exemplary eosinophil cells that	
				may be used according to these	
				assays include EOL-1 Cells.	
	HFGAJ16	537	Production of	MIP-lalpha FMAT. Assays for	A highly preferred
123			MIP1alpha	immunomodulatory proteins	embodiment of the invention
				produced by activated dendritic	includes a method for
				cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well known	embodiment of the invention
				in the art and may be used or	includes a method for inhibiting
				routinely modified to assess the	(e.g., reducing) MIP1a

production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,	described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammation disorders	Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma.	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate	chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of	chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T	used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	JR Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol

includes a method for stimulating (e.g., increasing) IL-4 production. An alternative	highly preferred embodiment of the invention includes a method	for inhibiting (e.g., reducing)	preferred indication includes	7	indication includes allergy. A	highly preferred indication	p		inflammatory disorders.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	melanoma, and/or as described	below under "Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	melanoma, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or
secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and	promote polarization of CD4+ cells into TH2 cells are well	known in the art and may be	used or routinely modified to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate imminomodulation, stimulate	immune cells, modulate immune	cell polarization, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for immunomodulatory	proteins evaluate the production	of cytokines, such as IL-4, and	the stimulation of immune cells,	such as B cells, T cells,	macrophages and mast cells.	Such assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,
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dysplasia. Preferred indications include blood disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic		Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,	suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an
"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194);	Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257- 261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the	contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in	the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance	responsiveness to immunomodulatory factors.

					infectious disease as described
					below under "Infectious
					Disease").
	HFIIA68	540	Activation of T-Cell	Kinase assay. JNK and p38	Preferred indications include
126)	p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
071			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative Disorders"),
				apoptosis are well known in the	blood disorders (e.g., as
				art and may be used or routinely	described below under "Immune
				modified to assess the ability of	Activity", "Cardiovascular
	_			polypeptides of the invention	Disorders", and/or "Blood-
				(including antibodies and	Related Disorders"), and
				agonists or antagonists of the	infection (e.g., an infectious
				invention) to promote or inhibit	disease as described below
				immune cell (e.g. T-cell)	under "Infectious Disease").
				proliferation, activation, and	Highly preferred indications
				apoptosis. Exemplary assays for	include autoimmune diseases
				JNK and p38 kinase activity that	(e.g., rheumatoid arthritis,
				may be used or routinely	systemic lupus erythematosis,
				modified to test JNK and p38	multiple sclerosis and/or as
				kinase-induced activity of	described below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and
				disclosed in Forrer et al., Biol	inflammatory disorders. Highly
				Chem 379(8-9):1101-1110	preferred indications also
-				(1998); Gupta et al., Exp Cell	include neoplastic diseases (e.g.,
				Res 247(2): 495-504 (1999);	leukemia, lymphoma, and/or as
				Kyriakis JM, Biochem Soc	described below under
				Symp 64:29-48 (1999); Chang	"Hyperproliferative Disorders").
				and Karin, Nature	Highly preferred indications

include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection,
410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.		Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of
	IFNg in Human T- cell 293T	Production of ICAM-1
	541	541
	HFKES05	HFKES05
	127	127

diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production.
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al., FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the
	Activation of transcription through serum response element in immune cells (such as T-cells).
	542
	HFKEU12
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Preferred indications include	described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in patients	with rheumatoid arthritis. An		indication is sepsis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative Disorders").	Additionally, highly preferred	indications include neoplasms	and cancers, such as, for
invention) to regulate the serum	response factors and modulate	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and Black	et al., Virus Genes 12(2):105-	117 (1997), the content of each	of which are herein incorporated	by reference in its entirety. T	cells that may be used according	to these assays are publicly	available (e.g., through the	ATCC). Exemplary mouse T	cells that may be used according	to these assays include the	CTLL cell line, which is an IL-2	dependent suspension culture of	T cells with cytotoxic activity.		
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example, leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for example,	hyperplasia, metaplasia, and/or	dysplasia. Preferred	indications include anemia,	pancytopenia, leukopenia,	thrombocytopenia, Hodgkin's	disease, acute lymphocytic	anemia (ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	neutropenia, neutrophilia,	psoriasis, suppression of	immune reactions to	transplanted organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication is	infection (e.g., an infectious
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					disease as described below under "Infectious Disease").
28	HFKEU12	542	IL-10 in Human T-cell 293T		
67	HFKFX64	543	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting or inhibiting immune cell proliferation. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include boosting an eosinophilmediated immune response, and

suppressing an eosinophil-	mediated immune response.																										-					
Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in the	late stage of allergic reactions;	they are recruited to tissues and	mediate the inflammatory	response of late stage allergic	reaction. Moreover, exemplary	assays that may be used or	routinely modified to assess the	ability of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils include	assays disclosed and/or cited in:	Zhang JP, et al., "Role of	caspases in dexamethasone-	induced apoptosis and activation	of c-Jun NH2-terminal kinase	and p38 mitogen-activated	protein kinase in human	eosinophils" Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al., "Disruption
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	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and
of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE
	Activation of transcription through cAMP response element (CRE) in pre-adipocytes.
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disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage	(e.g., due to diabetic neuropathy), blood vessel	impotence (e.g., due to diabetic neuropathy or blood vessel	blockage), serzures, mental confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular	Disorders" section below), dyslipidemia, endocrine	disorders (as described in the "Endocrine Disorders" section	below), neuropathy, vision	impairment (e.g., diabetic retinopathy and blindness),	ulcers and impaired wound	healing, and infection (e.g., infectious diseases and disorders	as described in the "Infectious	Diseases" section below,	especially of the urinary tract and skin), carpal tunnel
reporter assay may be used to identify factors that activate the cAMP signaling pathway.	adipogenesis, and is involved in differentiation into adipocytes.	CKE contains the binding sequence for the transcription factor CREB (CRE binding	protein). Exemplary assays for transcription through the cAMP response element that may be	used or routinely modified to test cAMP-response element	activity of polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) include assays disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm. Methods in Enzymol	216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch et	al., Mol Cell Biol 20(3):1008-1020 (2000); and Klemm et al.,	J Biol Chem 273:917-923	(1998), the contents of each of which are herein incorporated	by reference in its entirety. Pre-	adipocytes that may be used	according to these assays are publicly available (e.g., through

syndrome and Dupuytren's contracture). Additional highly preferred indications are complications associated with insulin resistance.		A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell
the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.		Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely
	HLA-DR in Human T cells	Activation of Natural Killer Cell ERK Signaling Pathway.
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also include cancers such as, kidney, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver, urinary cancer, lymphoma and leukemias. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS,	granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a
				MIP-lalpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the
				Production of MIP1alpha
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				HFRAB10
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production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as	described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases	(e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders.	Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary	assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and	the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol
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